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LESIONS OF THE CENTRAL AND PERIPHERAL NERVOUS SYSTEMS PRODUCED IN YOUNG RABBITS BY VITAMIN A DEFICIENCY AND A HIGH CEREAL INTAKE.

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IN previous publications [1 (*a*), (*b*), (*c*), (*d*), (*e*), (*f*)] accounts have been given of the dietetic methods whereby degenerative changes in the central and peripheral nervous systems of young dogs and rabbits can be produced and prevented. The two outstanding factors which, when associated together, produce these changes are: (1) A deficiency of vitamin A and carotene in the diet; and (2) a high cereal intake. Of these, the absence of vitamin A and carotene is probably the more important in young animals, for if either is added to the basal diets so far tested the degenerative changes do not occur. On the other hand, when vitamin A and carotene are deficient, the nerve degeneration can be made worse by altering the amount and type of cereal eaten, or in the dog by adding certain cereal products such as the embryo on ergot.

Except for one publication [1 (*c*)] in which the effects of vitamin A and carotene deficiency in producing xerophthalmia in rabbits were related to degenerative changes in the ophthalmic division of the trigeminal nerve, most of the published results referred to experimental work on dogs. It seemed desirable, therefore, that a fuller account should be given of the complex changes in nerve-cells and nerve-fibres which can be readily produced in young rabbits by similar dietetic means. Clearly, for a herbivorous animal like the rabbit, the basal diet must be of a different nature from that used in the dog experiments, and yet the same specific dietetic defects must be present in both.

Experiments were originally begun on rabbits with the object of discovering if possible the chemical nature of the substances in ergot and in cereals which act as neurotoxins in dogs and probably in man in

the absence of vitamin A and carotene. It was hoped that it would be easier to continue this part of the work on smaller and cheaper animals. Thus, it happened that the diet of many experimental rabbits in this series contained either ergot, or some extract or residue of this substance. As the work progressed, however, it became more and more questionable whether ergot affected the nervous system of rabbits even in the absence of the protective substances. In any case its neurotoxic action did not seem as potent in the rabbit as in the dog under the experimental conditions so far tested. It is certain that most, if not all, of the specific nervous lesions to be described can be readily produced in rabbits by withholding carotene and vitamin A and without giving ergot or ergot derivatives.

Although the present investigation has been fairly extensive and includes the examination of central and peripheral nerves as well as many groups of cells and ganglia in a large number of rabbits it is by no means complete. A neurological expert would undoubtedly find many other points of interest both in the behaviour of the animals and in the lesions of the nervous system produced by these specific nutritional conditions. This work, however, may lead others to extend the inquiry.

Experimental Conditions.

Litters of rabbits of eight to ten weeks old were used. The basal diets had to be such that they were compatible with good health and growth during the period in which the specific lesions developed. The following diet deficient in carotene and vitamin A was found to fulfil this object.

The main ingredients were 4 parts of oats and 1 part of bran to which calcium carbonate was added to form 1·5 per cent. of the mixture; lemon-juice was given in some of the experiments as a source of vitamin C. According to the age of the rabbit, 40 up to 70 grm. of the oats-bran mixture, together with a constant amount of 10 grm. of dried alfalfa which had been heated at 120° C. for thirty-six hours, were given daily. The alfalfa was ground to a fine powder and then heated in thin layers on trays in an electric oven and stirred frequently during the heating process in order to allow full exposure to the air. By this means its carotene content could be entirely destroyed. A point of importance for the production of severe lesions is the degree of destruction of the carotene in the alfalfa. If it be only partially destroyed, there may be little or no degeneration, or it may develop slowly and not be severe. For intense lesions to develop rapidly the heating and

stirring of the alfalfa must be sufficient to ensure the complete destruction of the carotene. If unheated instead of heated alfalfa be given, the nervous lesions do not appear. Similarly, if cabbage or carrots or any other source of carotene or vitamin A be added to the standard basal diet, the nervous system of the rabbit is protected. Pure carotene, in amounts of 1 to 3 mgm. daily, was sometimes added to the basal diet to prevent the nerve changes. In view of Stockman's results [2] in which he has produced derangement of the nervous system by diets rich in cereals but containing very little available calcium, it is necessary to point out that in the present work there is no deficiency of available calcium in the diet. It may also be well to add that in each series of experiments a rabbit with a normal nervous system has been produced by adding a source of the protective factor to the same basal diet as that given to the affected animal.

Behaviour of rabbits on the carotene-deficient diets.—The young rabbits grow and remain well on the basal diet for some months. The order of the appearance of signs of nerve defect varies, but slight stiffness of the legs, and especially of the hind legs, is generally the first abnormality noticed; this may be seen after two to three months of the experimental diets. Xerophthalmia appears next, three to six months after the beginning of the experiment; a dull patch or band appears on the cornea, usually in the centre, running midway between and parallel to the eyelids, i.e. in that part most exposed [1 (*e*)]. At this stage examination will show that the pupillary reactions are sluggish. Head movements usually develop quickly after this, although in some cases they are noticed before the changes in the eyes. The animal moves its head in a curious and characteristic way, as if it did not know its position in relation to the rest of the body; sometimes it is moved up and down and sometimes from side to side, and when at rest is often askew with ears awry. In the later stages of xerophthalmia some of the head movements may be due to ocular defects and obscured vision. The rabbit often moves about as if suffering from alcoholic intoxication. It may go round in circles, turn its head permanently towards one side, wobble from side to side, and in extreme cases even fall over either to the side or backwards, sometimes being unable to regain the normal position.

When examined in the cage the early signs are not so obvious; the animal has a sleepy look, the eyes often being half closed; it sits quietly huddled in the corner of its cage.

At no time is there any definite paralysis, but the animals appear

heavy on their legs and show less spontaneous movement both in the cage and outside, and in advanced cases often refuse to move at all.

It will be seen below that the lesions of the central and peripheral nervous systems are often very extensive, and no doubt a closer examination, especially tests on the sensory side, would reveal many other functional defects. A casual examination, however, makes it clear that the co-ordinating mechanism both of the head and body generally is defective, and in some cases it is obvious that the animals are blind and probably deaf.

Histological methods for demonstrating changes in nerve fibres.—Post mortem changes due to a lapse of time between death of the animal and fixation of its tissues were avoided. In some cases it was found better to fix the tissues *in situ*, but large organs and those with resistant capsules were dissected out and the tissues placed in the fixative.

A series of experiments on peripheral nerves was undertaken in order to compare the appearances produced by rough handling in post mortem dissection and those found in experimental animals. Nerves which were crushed with forceps, stretched or left for periods up to forty-eight hours after death of the animal gave positive Marchi reactions, but in these cases the appearances were not the same as those produced by lack of carotene or vitamin A. Needless to say, changes produced by trauma were avoided as much as possible.

The tissues were usually fixed in formalin (10 per cent. tap water neutralized formol saline).

Although methods have been used for observing changes in the axis cylinders, those for demonstrating degeneration of the myelin in the fatty sheaths have received most attention. These include: (1) Osmic staining by Marchi's method (with modifications); (2) Nile blue and sulphurous acid (Lorrain Smith [3]); (3) Scharlach R.

For peripheral nerves, on the advice of Sir Charles Sherrington, a method described by Ramon-y-Cajal [4] was also tested in the later experiments. Fresh nerves were stained for ten to sixteen hours in 0·5 per cent. osmic acid, washed in distilled water, treated with alcohol and glycerin, and then teased before microscopic examination. This method is only useful in the case of peripheral nerves, in which it shows up the changes very beautifully (Plate VI, figs. 5 and 6).

For the staining of axis cylinders several silver methods were tried, but sufficient experience of this technique was not obtained to warrant description of the results, especially of the earlier stages of axis cylinder degeneration, in the present publication. Changes certainly

are seen in the axis cylinders of the nerves of rabbits fed on carotene-deficient diets before advanced myelin degeneration occurs.

In order to determine the position of complete disappearance of groups of nerve fibres, Kulchitsky's modification of the Weigert-Pal method was adopted.

Observations on the Histological Results obtained by the above Methods.

When examining nerve fibres most attention was fixed on the myelin sheath and the changes it was liable to suffer under the prescribed experimental conditions. It is well known that histological methods for demonstrating demyelination changes, especially those involving the use of osmic acid, are apt to give unreliable results unless examined very critically. A great effort was made to avoid wrong interpretations of the experiments owing to misleading pictures; most of the animal experiments were repeated many times: the tissues from each animal were in many cases stained by several methods, and, when adopting any given technique for unknown tissues, sections of material known to be normal were often carried through simultaneously.

When the animals are severely affected there is no difficulty in demonstrating degenerative changes in the nervous tissues; when, however, the effects are slight it is by no means easy with the methods at present available. In early cases only two or three scattered fibres in a tract may be grossly changed; sometimes, for instance in the posterior roots, none show typical Wallerian degeneration, that found being rather of the annular type (see Plate VI, fig. 3). In this form the fibres are swollen, the myelin is altered in chemical composition but is not yet disintegrated, so that in cross section stained by Marchi's technique axis cylinders are seen surrounded by a dark ring of altered myelin stained with osmic acid. This annular type of degeneration is commonly found in the peripheral nerves of rabbits fed on carotene-deficient diets, but more rarely in the central nervous system. There is evidence that nerves so affected can be brought back to normal fairly rapidly when the deficient nutritive agent, in this case vitamin A or carotene, is supplied to the animal. This point, which I have discussed elsewhere [1 (*e*) (*f*)] in relation especially to degenerative changes in the ophthalmic division of the fifth nerve in cases of xerophthalmia, is one demanding much closer study both because of its scientific and its practical interest. When the degeneration is more advanced and the myelin sheath has disintegrated, structural recovery takes a much longer time.

The probable interpretation of the differences between the changes seen in the nerves of the carotene-deficient animals and those which are more familiar, namely, so-called Wallerian degeneration following injury when the axon is actually or virtually separated from its cell of origin, is that in the former the changes come on more gradually and are much more prolonged. The structural changes following nerve section are well known and the appearance of a fibre at different times after severance from its cell of origin can be more or less accurately foretold. For instance, fourteen to sixteen hours after section, Marchi's staining method will usually show the myelin sheath of the distal part of the nerve to be intact although stained with osmic acid; this, presumably the annular stage, is rapidly passed, however, and in the course of another eight hours the myelin sheath is breaking down and droplets are seen invading the axis cylinder. It seems probable, therefore, that the changes following injury and those caused by altered metabolism (toxic) differ only in degree and not in kind.

Toxic degenerative changes are much less understood, and, as regards the particular problems under discussion in this paper, have not previously been the subject of study. As might be expected from allied work on other animals, the time of onset and the degree of severity of the nerve lesions in rabbits fed on carotene-deficient diets varies. The age of the animal at the beginning of the experiment, the prenatal and postnatal feeding and probably the rate of growth and breed, all affect the results. The reason for these influences can in some cases be understood. For instance, it is obvious that a rabbit with large stores of vitamin A in the liver at the time of the initiation of the experimental feeding will resist longer the influence of a carotene-deficient diet than one with only small stores of this substance. Similarly, a rapidly-growing animal might be expected to use up its stores more quickly. But some of the factors influencing the rate and severity of the onset, especially the question of age, are more difficult to understand. Age seems to bring about a greatly increased stability of the nervous system, and an adult animal is very resistant to the dietetic influences discussed here which in younger animals rapidly result in extensive degenerative changes in parts of the nervous system.

In some experiments in the series the animals were killed soon after the general signs of abnormality were first observed; in others a longer interval was allowed so that degeneration was more extensive. Sometimes, after the morbid condition had been produced, a source of carotene or vitamin A was added to the diet, with the result that further

degeneration was prevented and curative changes were observed. This part of the problem will be discussed in a later paper.

Distribution of nerve degeneration in carotene deficient rabbits.—An account will now be given of the more common positions of the different levels of the brain and cord in which lesions are found in rabbits brought up on diets previously described where vitamin A and carotene are deficient. As it is not easy to take low-power photomicrographs of Marchi preparations which show up the degenerated fibres, it was decided to make drawings showing the position and relative amount of degeneration at representative levels. At first it was thought that this would give as accurate a record as the work justified. On further consideration, since it seemed certain that some at least of the fibres involved in more obvious lesions could be identified, as those of the dorsal columns and of the spino-cerebellar tracts, attempts were made to associate more and more of the degenerated fibres with well recognized tracts. This procedure became more necessary when the medulla, pons and mid-brain were examined, as it was desirable if possible to make some kind of a unified story out of what at first sight seemed a mass of disconnected facts. The distribution of the degenerated fibres in the medulla and pons has helped considerably in the identification of degenerated fibres in the cord, for many tracts which are in close proximity in the latter separate out in the higher regions and therefore can be more readily differentiated. I have therefore attempted to describe the actual degenerative changes in terms of well-recognized tracts, in spite of the fact that in so doing some errors may have been made.

Although the brain-stem of the rabbit is built up on the same plan as that of other mammals, variations in the size and position of some of its component parts are apt to lead to difficulty in recognizing certain groups of nerve fibres and nerve cells (nuclei). For instance, the inferior olivary proturbances in the rabbit are small as compared with those of man. Again, in the human brain a large band of transverse pontine fibres are seen superficially, while in the rabbit the pons is a relatively small structure (see fig. 1) so that these fibres form a comparatively narrow band. Before attempting to identify the lesions in the affected animals, it was thought desirable to fix the "land marks" of the brain of the rabbit as compared with other mammals and for this purpose serial sections (30μ thick) were made right through the brain of a normal animal. Every tenth section was stained with hæmotoxylin after mordanting, so that a general view of the main anatomical and

histological arrangements in the rabbit's brain was obtained (fig. 1) and compared with similar levels in man and dog.

Even when the general relationship of the larger features of the brain are grasped, differences in the relative number and position of fibres forming established tracts in different species also bring difficulties in describing lesions in detail. The rabbit, in common with many other mammals, has no direct pyramidal tract in the ventral column so that the intense degeneration in this column, and especially in the fibres adjacent to the ventral fissure so commonly seen in the affected rabbits in this work, cannot belong to the direct pyramidal tract. Corroboration of this deduction is obtained by the fact that even in fairly severely

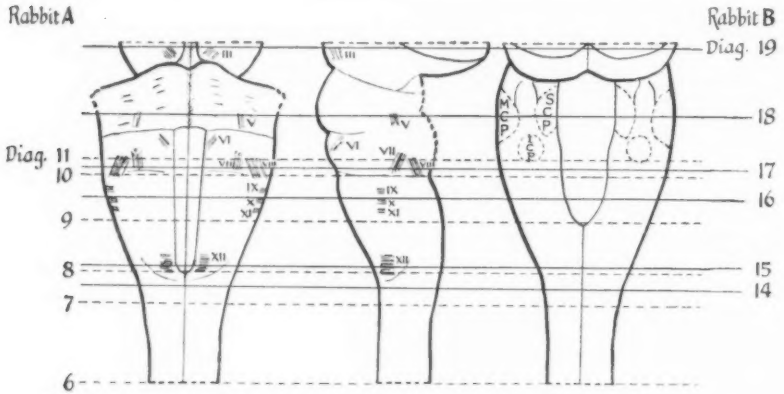

FIG. 1.—Diagrams of dorsal, lateral and ventral aspects of a rabbit's brain-stem to show the relative positions of diagrams 6-11 (rabbit A) and 14-19 (rabbit B).

affected animals it is rare to find degenerated fibres in the pyramidal tract of the pons and medulla, or in the crossed pyramidal tract of the cord.

A still further difficulty in interpreting lesions of the brain-stem is that, although the main tracts in the central nervous system of man and some animals have long been established, there are still many groups of neurons of whose origin, distribution and termination little is known, and this seems to be especially true in the case of some common laboratory animals like the rabbit and rat.

In face of these difficulties it may be necessary to amend the names given here to some of the degenerating tracts; the positions indicated in the figs. 3 to 19, however, represent the lesions as found in the majority of the experimental animals fed on carotene-deficient diets.

In view of the varied nomenclature adopted by different workers to distinguish any one tract, it may be well to add that in this publication: (1) The terms lumbar, thoracic and cervical have been used for the three main regions of the cord; (2) that in cross-sections of the cord the three main divisions into which the long fibres are broken by the gray matter are referred to as the dorsal, lateral and ventral columns; (3) as far as possible the names used for the tracts indicate the origin and destination of the fibres. When two groups of fibres are found in different positions and yet have the same endpoint and the same origin they are referred to as ventral, dorsal or lateral in relation to each other, e.g. ventral spino-cerebellar and dorsal spino-cerebellar (both in lateral columns), also ventral spino-reticulo-thalamic (ventral column) and lateral spino-reticulo-thalamic (lateral column) (see fig. 2).

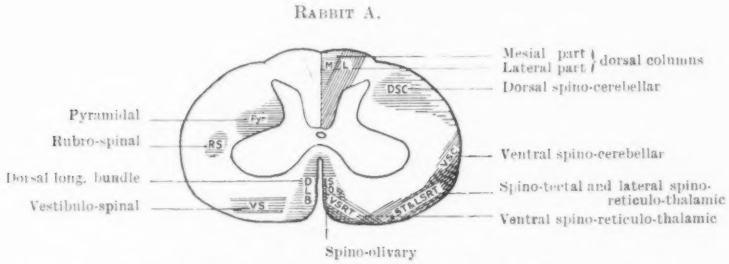

FIG. 2.—Rough diagrammatic representation of the position of the main tracts in a rabbit's spinal cord.

The drawings seen in figs. 3 to 19 were made from representative sections (stained by a modified Marchi method) of the cord and brain-stem of two rabbits (A and B) in which severe signs developed. Sometimes a section of one of these rabbits reveals the points it is desired to emphasize better than those of the other. The first animal A, shows much degeneration of the cerebellar tracts, whilst in the second animal B, most degeneration was found in the fillet. The diagrams do not represent the distribution of degenerated fibres in all the animals of this large series of experiments; they demonstrate, however, the positions in which degeneration is more commonly found.

Both rabbits had the same carotene-deficient diet (one had a daily addition of untreated and the other of treated ergot). In A the earliest symptoms appeared about the twelfth week and by the twenty-second week there was definite though slight inco-ordination. Xerophthalmia and head movements were seen about the twenty-third week, and by the

twenty-fifth the animal was very inco-ordinate and had difficulty in regaining its balance when put on one side. It was killed on the twenty-eighth week, sixteen weeks after the first signs of nervous abnormality. The second animal B was on diet only eight weeks when it showed the first signs of abnormality, especially slight stiffness and head movements. These gradually increased although there was slight improvement over one period. After the twenty-first week its head was held permanently to the left and there was definite xerophthalmia. It was killed after twenty-five weeks (seventeen weeks after appearance of the first signs), when the inco-ordination was great and the head-jerks such that the animal tended to fall over backwards.

An examination of figs. 3 to 19 shows the distribution of degenerated fibres and tracts in the spinal cord and brain-stem. In these drawings, black dots represent degenerating fibres as revealed by Marchi method, circles "o" represent fibres which have completely degenerated, and not annular degeneration (see p. 145).

I.—Spinal Cord.

Ascending tracts.—In the spinal cord degeneration is found in the following ascending paths:—

(1) In both tracts of the dorsal columns. It is more common to find degeneration in the lateral than in the mesial column.

(2) In the following tracts of the lateral columns:—

(*a*) dorsal spino-cerebellar;

(*b*) lateral spino-reticulo-thalamic;

[There is reason to believe that the ventral and lateral spino-thalamic tracts consist in part of fibres with synaptic interruptions, especially in the reticular formation of the brain-stem, and the two tracts are sometimes designated as the spino-reticulo-thalamic paths (Page May [5].]

(*c*) ventral spino-cerebellar; and

(*d*) in the spino-tectal;

[The fibres of this tract are in the cord associated with the lateral spino-reticular-thalamic tract, but it forms a separate tract in the mid-brain where degenerated fibres are seen (figs. 12 and 19).]

(3) In the ventral columns the most prominent ascending degenerated fibres belong to: (*a*) ventral spino-reticular thalamic (see note 2*b* above); and (*b*) possibly spino-olivary tracts.

Descending tracts.—There are degenerated fibres in the following descending tracts of the spinal cord: (*a*) the rubro-spinal; (*b*) vestibulo-

spinal; (*c*) the dorsal longitudinal bundle. The extent of the dorsal longitudinal bundle in the rabbit is not definitely established.

The main descending tract, namely the crossed pyramidal, is usually quite free from degenerated fibres, although in some of the carotene-deficient rabbits a few degenerated fibres are occasionally found in what is apparently the crossed pyramidal tract.

It is interesting to note in connection with the obvious impairment of equilibrium in these rabbits that all the degenerated descending fibres so far identified are connected with the vestibular and cerebellar systems.

II.—Brain-stem.

Ascending tracts.—In the brain-stem degeneration is found in the upward continuation of the ascending tracts of the spinal cord, including: (*a*) The dorsal spino-cerebellar, the degenerated fibres of which can be traced into the restiform body; (*b*) the ventral spino-cerebellar, fibres from which are seen entering the cerebellum via the superior peduncle; (*c*) the lateral and ventral spino-reticulo-thalamic tracts which pass close together through the brain-stem directly, or indirectly, to the thalamus; (*d*) spino-olivary; (*e*) degeneration is also found in the mesial fillet (composed largely of axons of cells in the nucleus gracilis and cuneatus); (*f*) in the lateral fillet which includes the second neurons of the auditory path; (*g*) the ascending fibres of the dorsal longitudinal bundle which connects the vestibular nuclei with the 3rd, 4th and 6th nuclei.

Descending tracts.—The descending tracts of the brain-stem showing degeneration include: (*a*) Rubro-spinal. Some degeneration is seen in the mid-brain where the fibres decussate (figs. 12 and 19) and in the medulla; in the pons and cord they are difficult to distinguish from degenerated fibres of other tracts; (*b*) vestibulo-spinal; (*c*) dorsal longitudinal bundle (below the vestibular nuclei).

Degenerated fibres are also seen in the intra-medullary portion of some of the sensory cranial nerves, especially the 8th and 5th.

It is interesting to compare and to contrast the behaviour during life with the amount of degeneration in the dorsal longitudinal bundles (vestibular connections) in these two animals: the head movements came on earlier and were much more pronounced in rabbit B than in rabbit A. Corresponding with this there was more degeneration in the dorsal longitudinal bundle of rabbit B. There was in rabbit A an access

of degenerated fibres in the dorsal columns at the lowest medulla level (fig. 7) (compare with the dorsal column of Cervical II (fig. 6)).

In examining the individual drawings and comparing them with one another, it will be seen that the actual and relative number of degenerated fibres in many tracts vary in the different segments.

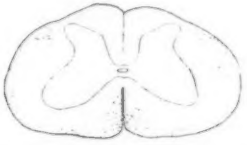

FIG. 3.—Lumbar, Segment IV.

FIG. 4.—Thoracic, Segment VII.

FIG. 5.—Cervical, Segment VI.

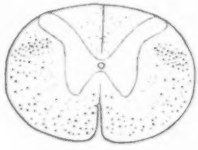

FIG. 6.—Cervical, Segment II.

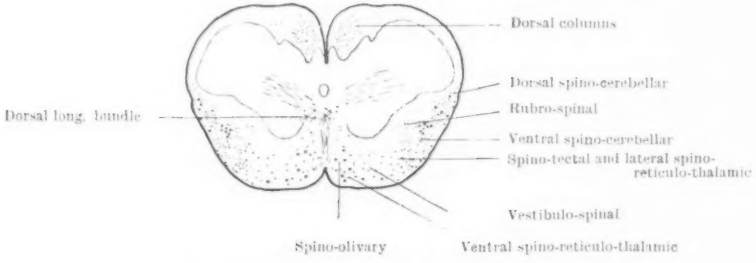

FIG. 7.—Medulla, pyramidal decussation.
Drawings illustrating degeneration in brain-stem and spinal cord of a rabbit on a carotene-deficient diet.

The following lesions were seen in the brain and cord of rabbits A and B.

Lumbar Segment IV (rabbit A) (fig. 3).—There are very few degenerated fibres in the dorsal columns; more are found in the cerebellar tracts and in the ventral columns adjacent to the ventral fissure. There is less degeneration in the lumbar and sacral regions than in any other levels examined. This is in general true for all rabbits fed on these carotene-deficient diets.

Thoracic Segment VII (rabbit A) (fig. 4).—There are many more degenerated fibres in this level than in lumbar IV. Dogs brought up on diets

deficient in vitamin A and carotene often had comparatively few degenerated fibres in the thoracic cord [1 (*c*)].

Cervical Segment VI (rabbit A) (fig. 5).—In this region the degeneration seems to have reached its maximum in the cerebellar and ventral column tracts, while the dorsal columns appear to contain fewer degenerated fibres than in the thoracic levels.

Cervical Segment II (rabbit A) (fig. 6).—The main change usually seen in this region is the scattered appearance of the degeneration in contrast to that in the lower levels of the cord; this is partly because the ascending tracts are separating out in preparation for redistribution in the brain-stem. At this level the degeneration in rabbit A is more evenly distributed between the lateral and mesial parts of the dorsal columns than is generally seen.

Medulla, pyramidal decussation (rabbit A) (fig. 7).—At the level of the motor decussation many degenerating fibres are seen in the dorsal columns near the nuclei cuneatus and gracilis, and also in the dorsal and ventral spino-cerebellar and lateral spino-reticulo-thalamic tracts. Rather less degeneration is seen in the white matter which includes the ventral spino-reticulo-thalamic, spino-tectal and spino-olivary tracts.

The fibres of the ventral columns naturally assume a more lateral position owing to the decussation of the pyramids, none of the fibres of which are affected, although some transversely cut fibres between the decussating ones are degenerated. These probably belong to the dorsal longitudinal bundle; there is some degeneration in what appear to be the vestibulo-spinal and the rubro-spinal tracts.

For the sake of clarity reference will first be made to some of the higher levels of rabbit A, then a few sections of rabbit B will be described.

Medulla, higher part of sensory decussation (rabbit A) (fig. 8). The inferior olivary and lateral reticular nuclei are just appearing at this level. Degenerated fibres are present in the remains of the dorsal columns, although many fibres have entered the nuclei gracilis and cuneatus. The axons of some of these cells can be seen sweeping through the reticular formation as internal arcuate fibres. There is much degeneration in the dorsal and ventral spino-cerebellar tracts but little in the mesial fillet (cf. fig. 15). The spino-reticulo-thalamic (above the level of the pyramidal decussation the lateral and ventral spino-reticulo-thalamic appear to run together), spino-tectal and possibly also the spino-olivary tracts contain some degenerated fibres and remain in approximately the same positions as in fig. 7. Of the descending fibres the dorsal longitudinal bundle and rubro-spinal tract show some degeneration; the vestibulo-spinal, still obscured by other tracts, is probably degenerated whilst the pyramidal is unaffected. The 12th nerve containing no degenerated fibres is seen passing ventralwards through the section.

Medulla, level of inferior olivary nucleus and the 4th ventricle (rabbit A) (fig. 9).—At this level in rabbit A there is not much degeneration in the fillet,

but there is still heavy degeneration in the dorsal spino-cerebellar tract which is moving towards and entering the restiform body, the ventral spino-cerebellar, the spino-reticulo-thalamic and the spino-tectal tracts. There is some, but not

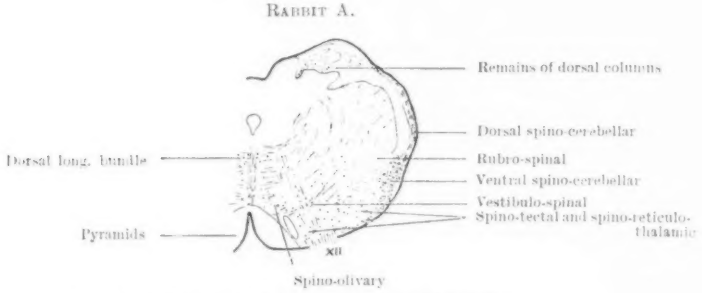

Fig. 8.—Medulla, higher part of sensory decussation.

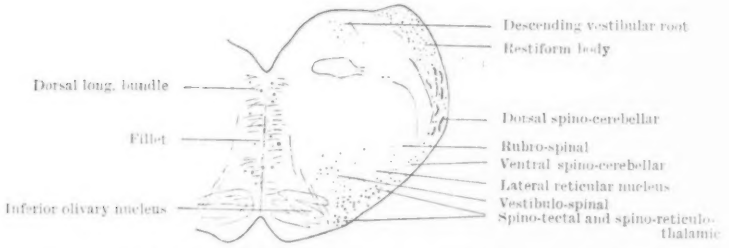

Fig. 9.—Medulla, level of inferior olivary nucleus and 4th ventricle.

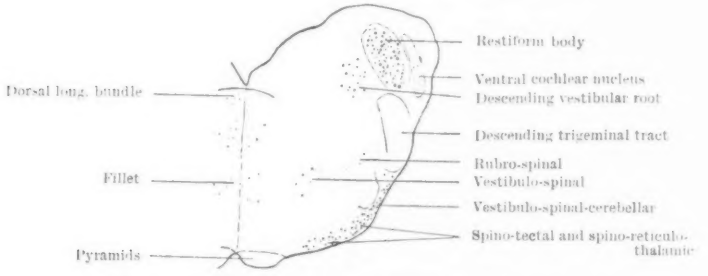

Fig. 10.—Section between medulla and pons.

Drawings illustrating degeneration in brain-stem and spinal cord of a rabbit on a carotene-deficient diet.

much, degeneration in the dorsal longitudinal bundle; of the other descending tracts, the vestibulo-spinal and what appears to be the descending vestibular root of the 8th nerve contain more degenerated fibres. The latter has only been

traced as low as the higher levels of the nuclei gracilis and cuneatus. Some small degenerated fibres are present in the position of the rubro-spinal tract. It is interesting to note that in this animal there are degenerated fibres among the cells of the lateral reticular nucleus. These are only found in animals having much degeneration in the lateral cord columns and the restiform body. Rabbit B, which has less degeneration in the lateral tracts, does not show any degenerating fibres among these cells. The lateral reticular nucleus is said to relay impulses from the lateral tracts of the cord to the restiform body.

Section taken between medulla and pons (rabbit A) (fig. 10). The transverse pontine fibres are not seen although this section is taken above the level of the inferior olivary nuclei. A few fibres of the mesial fillet are affected. The large group of degenerated fibres on the latero-ventral aspect belong to the ventral spino-cerebellar, the spino-reticulo-thalamic and spino-tectal tracts. There is much degeneration in the restiform body, mainly dorsal spino-cerebellar fibres. Degeneration is seen in the dorsal longitudinal bundle, vestibulo-spinal tract, the descending vestibular root and also in a few fibres of the rubro-spinal tract. The pyramids are free from degeneration, as also is the descending branch of the 5th nerve. (In one or two experiments this branch of the 5th nerve contained degenerated fibres.) Degenerated fibres are also found among the cells of the ventral cochlear nucleus.

Level of the 8th and 7th nerves (rabbit A) (fig. 11).—In this section the transverse fibres of the trapezoid body can be seen. These, some of which are degenerated in rabbit A, arise in cells of the ventral cochlear nucleus and form the greater part of the lateral fillet of the opposite side (second neurons of the auditory path). The pyramidal tract contains no degenerated fibres and remains at the ventral surface of the brain-stem. The degenerating fibres of the ventral spino-cerebellar tract can be seen between the 7th and 8th nerves, bearing dorsalwards to enter the superior cerebellar peduncle. The restiform body has already entered the cerebellum in spite of the fact that the pons is not yet established. There is now much less degeneration in the ventro-lateral region since the ventral spino-cerebellar tract has moved dorsalwards and some of the spino-reticulo-thalamic fibres have probably entered relay stations in the reticular formation of the medulla. The only descending tracts in which degenerated fibres appear are the dorsal longitudinal bundle and the rubro-spinal. This section, being at the level of the 8th nerve, shows no descending vestibular root or vestibulo-spinal tract. Heavy degeneration is seen in the 8th nerve, while the 7th and 6th are unaffected.

Superior corpora quadrigemina (rabbit A) (fig. 12).—The only ascending tract containing degenerated fibres at this level is the spino-tectal. The others which showed degeneration in fig. 11 have probably entered relay stations; for instance, the spino-reticulo-thalamic fibres of the lower levels may have made synapses with cells in the reticular formation of the medulla and pons, some fibres of the lateral fillet have probably entered the nucleus of this fillet, and the ventral spino-cerebellar tract has entered the cerebellum via the superior cerebellar peduncle. Degeneration is, however, seen in the dorsal

longitudinal bundle and in the rubro-spinal decussation. A few fibres of the 3rd nerve also take up Marchi stain. Although there is no degeneration in the internal capsule or the pyramidal tract of the lower brain stem, there are a few degenerated fibres in the crusta of this level.

Cervical, Segment II (rabbit B) (fig. 13).—It has previously been noted

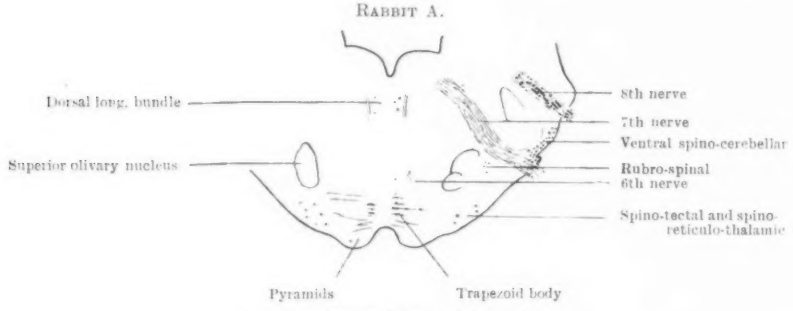

Fig. 11.—Level of 8th and 7th nerves.

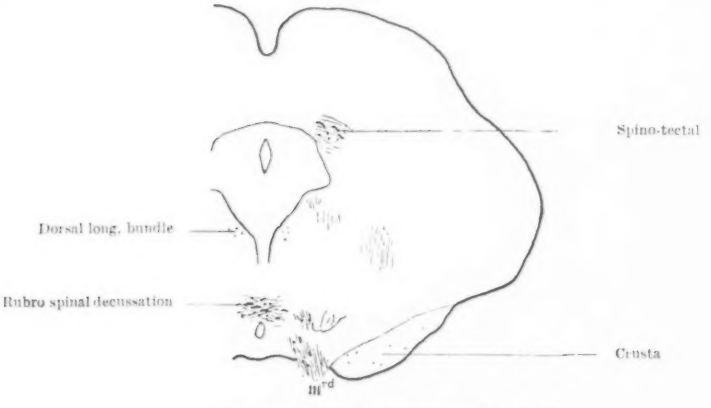

Fig. 12.—Superior corpora quadrigemina.

Drawings illustrating degeneration in brain-stem and spinal cord of a rabbit on a carotene-deficient diet.

that in rabbit B the degeneration is most prominent in the fillet and dorsal longitudinal bundle, whereas in rabbit A the heaviest degeneration is in the cerebellar tracts. This can be seen by comparing figs. 6 and 13. In rabbit B many fibres of the dorsal columns show very advanced degeneration with absorption of the myelin, and, as might be expected, there is also advanced degeneration of the second neurons of this path in the mesial fillet but no

RABBIT B.

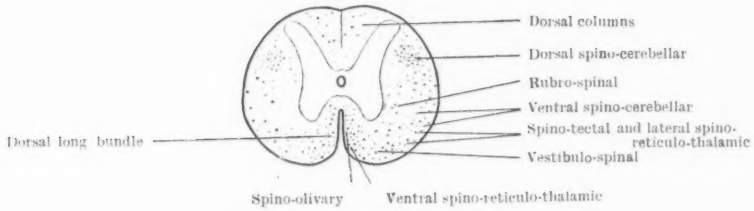

FIG. 13.—Cervical, Segment II.

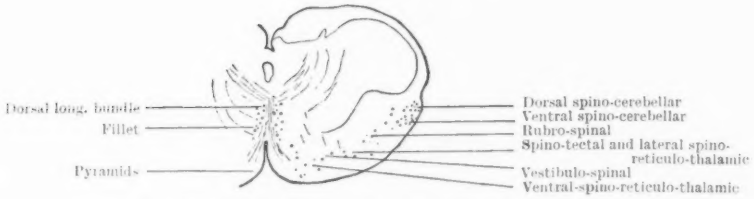

FIG. 14.—Medulla, lower part of sensory decussation.

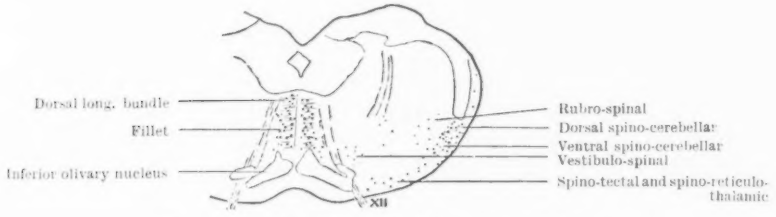

FIG. 15.—Medulla, level of inferior olivary nucleus.

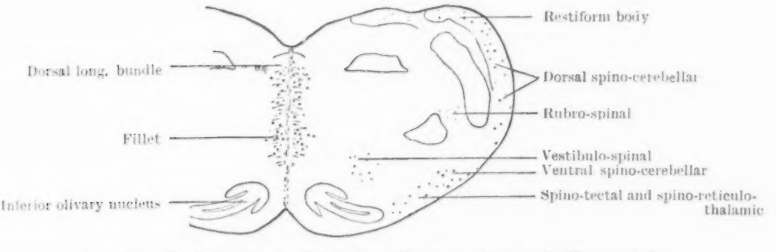

FIG. 16.—Medulla, level of inferior olivary nucleus and 4th ventricle.

Drawings illustrating degeneration in brain-stem and spinal cord of a rabbit on a carotene-deficient diet.

evidence of degeneration in a third neuron has been found either in this rabbit or in any others of the series so far examined.

Medulla, lower part of sensory decussation (rabbit B) (fig. 14).—Ascending degeneration is seen in the fillet, in the ventral spino-reticulo-thalamic tract, in the dorsal and ventral spino-cerebellar tracts, in the lateral spino-reticulo-thalamic, in the spino-tectal and possibly the spino-olivary tracts. Descending fibres in the dorsal longitudinal bundle, the vestibulo-spinal and the rubro-spinal tracts are degenerated. At this level the dorsal longitudinal bundle and the vestibulo-spinal tract can be seen in separate bundles, while in the cord they could not be clearly differentiated from other tracts.

Medulla, level of the inferior olivary nucleus (below 4th ventricle) (rabbit B) (fig. 15).—In this section there is much degeneration in the fillet and also some in the dorsal spino-cerebellar tracts, but less than in rabbit A. The ventral spino-cerebellar, spino-reticulo-thalamic and spino-tectal tracts contain some degenerated fibres which are seen in the same positions as in fig. 8. Degenerated fibres of the vestibulo-spinal tract appear dorsal to the inferior olivary body. The dorsal longitudinal bundle and the rubro-spinal tracts containing degenerated fibres retain the same relative positions. There is no degeneration in the pyramids. So far, degeneration has not been found in the 12th, 11th, 10th or 9th nerves.

Medulla, level of inferior olivary nuclei and 4th ventricle (rabbit B) (fig. 16). Degenerated fibres of the mesial fillet are the most prominent features of this section, degeneration being heavier than in any other of the ascending tracts. The dorsal spino-cerebellar, ventral spino-cerebellar, spino-reticulo-thalamic and spino-tectal tracts contain some degenerated fibres. The dorsal longitudinal bundle and vestibulo-spinal tracts are the most severely degenerated of the descending fibres, but the descending vestibular root and the rubro-spinal tracts are also affected. In contrast to fig. 9 (rabbit A) there are no degenerated fibres among the cells of the lateral reticular nucleus. The pyramids are again without degenerated fibres.

Level of 8th nerve (rabbit B) (fig. 17).—This section shows degenerated ascending fibres in the fillet, restiform body, spino-reticulo-thalamic, ventral spino-cerebellar and spino-tectal tracts. Degenerated descending fibres are seen in the dorsal longitudinal bundle, vestibulo-spinal and rubro-spinal tracts. The pyramids are again unaffected. Roots of the 8th and 7th nerves can be seen and many degenerated fibres are present in the former, but none in the latter.

Pons, 5th nerve level (rabbit B) (fig. 18).—Degeneration can be seen in the regions of the spino-reticulo-thalamic and spino-tectal tracts. The degenerated fibres of the restiform body have disappeared, and the degenerated ventral spino-cerebellar tract is now coursing towards the superior cerebellar peduncle. Degenerated fibres can be seen in the dorsal longitudinal bundle and what are presumably the rubro-spinal and vestibulo-mesencephalic tracts. The pyramids are again free from degeneration. Degeneration can be clearly seen in the fibres of the 5th nerve.

Posterior part of superior corpora quadrigemina (rabbit B) (fig. 19).—Much less degeneration is present in this section than in fig. 18. No degeneration is

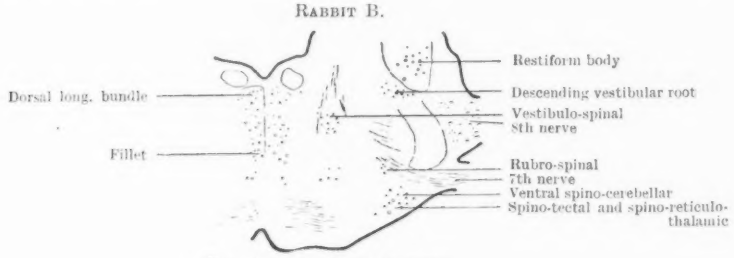

Fig. 17.—Level of 8th nerve.

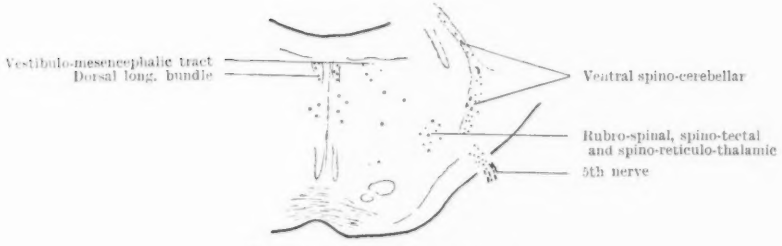

Fig. 18.—Pons, 5th nerve level.

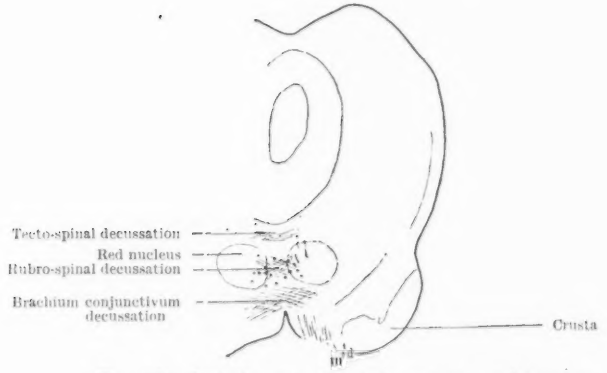

Fig. 19.—Posterior part of superior corpora quadrigemina.

Drawings illustrating degeneration in brain-stem and spinal cord of a rabbit on a carotene-deficient diet.

seen in the ascending tracts of this region, as they have probably entered relay stations. Degenerated fibres are present in the dorsal longitudinal bundle and in the decussation of the rubro-spinal tract.

Degenerative Changes in Peripheral Nerves.

Extension of the investigation to the peripheral nerves was begun because the inco-ordination of the animals, and especially the movements of the head, often appeared greater than might be expected from the extent of lesions of the central nervous system. For this reason the vestibular divisions of the 8th nerve were first examined and it soon became obvious that this nerve suffered greatly in the animals receiving the carotene-deficient diets. This is illustrated in Plate IV, fig. 1. Not only are the extra-medullary parts of these nerves degenerated, but intra-medullary fibres are also affected. (Plate V, fig. 1.) The degeneration in the 8th nerve accounts largely for the inco-ordination of the head movements so often seen in carotene and vitamin A deficient animals. Fig. 2 shows the normal when cabbage was included in the diet.

The cochlear division of the 8th nerve was then examined, and here again changes were revealed, which are illustrated in Plate IV, figs. 3 (*a*) and (*b*). It will be seen that while the rabbit receiving carrots (figs. 4 (*a*) and (*b*)) has a normal nerve, that of the carotene-deficient animals contains fibres with extensive myelin changes (figs. 3 (*a*) and (*b*)). Similar differences were also seen in that part of the cochlear nerve which passes through the cochlear bone. Preparations were made after decalcification of the bone. A point of special interest is the round-cell infiltration within the bony cochlear found in the carotene-deficient animal and the absence of these cells from the control. The results obtained leave little doubt that the cochlear nerve is very susceptible in these young rabbits to the special nutritional defect under examination.

Degenerating fibres were also found in the optic nerves of the carotene-deficient animals (Plate V, figs. 3 and 4). I have shown elsewhere [1 (*b*)] that these changes were sometimes so severe in dogs which have been fed for several years on a vitamin A and carotene-deficient diet that all the fibres of the optic nerve have disappeared. This aspect of the subject I propose to deal with at greater length in another publication because of its possible relationship to retrobulbar neuritis and night blindness, the latter a well-recognized result of vitamin A and carotene deficiency.

The other sensory nerve of the eye—the ophthalmic division of the trigeminal nerve—has been discussed in full previously, more particularly in relation to xerophthalmia [1 (*e*)]. It was there shown that degeneration of this nerve and xerophthalmia are associated, and that the latter can probably be regarded as due to a loss of neurotrophic control.

It is evident that these investigations on the optic and trigeminal nerves, by supplying a common basis in the form of afferent nerve defect due to a specific dietetic deficiency, offer an explanation for two pathological conditions affecting the eye, night blindness and xerophthalmia, two conditions which at first sight seem to have no relation to one another.

One other sensory nerve of the head, namely, the inferior dental nerve, has also been the subject of inquiry by M. Mellanby and J. D. King [6], who have shown that vitamin A and carotene deficiency bring about, in young rats, dogs and rabbits, degenerative changes in it. They also found evidence that these

demyelination changes were related to hyperplasia of the epithelium of the gum margin, especially of the part adjacent to the teeth, and the subsequent invasion of the epithelial cells by micro-organisms resulting in pyorrhœa, a disease which develops in animals eating a cereal diet deficient in vitamin A and carotene [7].

Thus it is evident that all the sensory nerves of the head so far examined in young rabbits are affected by carotene deficiency, including both auditory and vestibular branches of the 8th nerve, sensory branches of the 5th nerve to the eyes and teeth and the optic nerve. On the other hand the motor cranial nerves were normal in the experiments so far completed at a time when the sensory nerves of the head showed great demyelination changes; a few degenerated fibres, however, have been occasionally seen in the 3rd nerve (fig. 12).

In view of the almost clear-cut division between the susceptibility of the sensory and motor cranial nerves, it was a matter of interest to see whether other afferent and efferent nerves behaved similarly under these dietetic conditions. Sciatic nerves which contain both efferent and afferent fibres are affected by carotene deficiency (compare figs. 5 and 6 of Plate V). On the analogy of the cranial nerves it seemed likely that the afferent fibres would be affected and that the motor fibres would escape. This is the case in the majority of the experiments for, in the rabbits brought up on carotene-deficient diets and showing typical signs of the deficiency, the ventral roots (motor) were usually free from myelin degeneration, whereas the dorsal roots were always affected (Plate VI, figs. 1 to 4). Both roots of the animal fed on cabbage are devoid of degeneration, whereas in the animal not receiving carotene the dorsal root shows much degeneration, whilst the ventral root is normal. This is the usual result, but in animals where the dietetic defect has continued for a long time some of the ventral root fibres also may be degenerated. The affection of the dorsal roots can be clearly demonstrated by Cajal's osmic method (Plate VI, figs. 5 and 6). When the rabbit had the basal diet only, the degenerative changes are obvious (fig. 5), but when a few drops of concentrated vitamin A oil (0·1 c.c. = 100 blue values), were added to the diet the fibres are normal (fig. 6).

Reference has been made above to the vagus nerve. It might be expected that, although the motor fibres in this nerve would escape, its afferent fibres would suffer in the same way as most of the other afferent nerves. This has not been found to be true; in spite of many examinations of these nerves, even in severely affected animals, no degenerative changes have so far been seen in them. In rats brought up on a vitamin A deficient diet, Zimmerman [8] found some degeneration in the vagus nerves in only four out of eight animals examined, but in all there was extensive degeneration of the medullary sheaths of the brachial plexuses and sciatic nerves.

There is still a wide field left for future observation as regards these nerve changes. It is known that both the skin and epithelial surfaces are particularly susceptible to infection in vitamin A deficiency, and epithelial surfaces also

develop characteristic changes as hyperplasia and keratinization of their cells. On the analogy of the eye (xerophthalmia) and the gums (periodontal disease) it is probable that these epithelial changes are related to degeneration of the corresponding afferent nerves. It would be of interest to know whether the afferent nerves from joints and muscles are also affected by the dietetic deficiency under examination, and, if they are so affected, whether specific lesions are produced in these end organs which correspond to the pathological changes developing in the skin and epithelial surfaces.

Nerve-Cells.

In view of the great degenerative changes in the conducting fibres of the cord resulting from these specific nutritional defects, it is not surprising that many cells are also affected. Indeed, it is not improbable, considering the differentiation between the widespread degeneration of the intermedullary ascending fibres and the afferent nerves and the comparative immunity of the descending tracts and the efferent nerves, that many of the primary effects of the abnormal nutrition under consideration are on the cells and that the changes in the nerve fibres are secondary.

In spite of the large amount of work done by many investigators on the morbid anatomical changes of nerve-cells, there still remains a general lack of systematized knowledge as to the relation of the structures seen under the microscope after fixation and other treatment and their functional state during life. Nissl's bodies found in suitably stained sections vary in size, shape and arrangement in the different nuclei of any one species, and in different species cells having the same functions often vary greatly in appearance. This introduces a difficulty into the interpretation of experimental results even when care is taken to use controlled and efficient methods of fixation and to avoid post mortem and manipulative changes. However, when all technical errors in preparation have been avoided and all the processes are carried through as far as possible under identical conditions, there is no doubt at all that there are greater differences in the microscopical appearances of the nerve cells of the carotene-fed and carotene-free animals than can be accounted for by normal variations.

When nerve-cells undergo degenerative changes as the result of lesions of their axons, the process is usually called secondary degeneration. Cell changes brought about by toxic agents are known as primary degenerations. This phraseology was introduced by Marinesco.

Secondary degeneration of the nerve-cell due to injury of its axon, and particularly the changes in the chromophile elements, was discovered by Nissl [9]. It consists of a breaking up of the chromophile elements

first beginning round the nucleus, a swelling of the whole cell and a movement of the nucleus towards the periphery. All nerve-cells whose conducting fibres are cut do not react in this way. The best reactions are seen in motor cells, as those of the ventral horns or in the cortical motor cells, when their respective conducting fibres suffer transection. Peripheral afferent nerve-cells, as those of the dorsal root ganglion, undergo secondary degeneration when the peripheral portions of the fibres are divided, but not when their central processes, i.e. the dorsal roots, are injured.

In the central nervous system itself, apart from the chromolysis and other changes seen in the cells of Clarke's column when the dorsal spino-cerebellar tract is destroyed, but little is known of secondary cell changes in ascending systems. It is certain, however, that afferent cells in the central nervous system are by no means as susceptible to this type of change as the motor cells.

The question of primary or toxic reactions of nerve-cells, the so-called primary degenerations, is even more complex. Since the introduction of the Nissl technique, many investigations have been made to determine the changes produced in nerve-cells by known toxic substances. Nissl [11] himself investigated the action of many such substances including lead, arsenic, phosphorus, mercury, silver, alcohol, morphine, bromide, cocaine, trional, veratrine, strychnine, carbon disulphide, and tetanus toxin. Goldscheider and Flatau [12] also made many investigations into the effect of pathological conditions produced experimentally on nerve-cells. Russell [13] has studied the effect of parathyroidectomy on cells of the nervous system, and in more recent times Dye [14] has compared the effect of parathyroidectomy and cretinism on the nerve-cells of dogs. Other harmful procedures whose effects on nerve-cells have been studied include ischæmia, inanition, hyperpyrexia, uræmia, extirpation of the suprarenal bodies, and experimental and natural infection.

Although it is undoubted that nerve-cells undergo changes under many of the above conditions, the subject of primary degeneration has remained generally unsatisfactory aud undeveloped. One of the difficulties in work of this nature is, as Nissl himself recognised, that under conditions which produce primary degeneration of the nerve-cells even one group may show the widest variations, some appearing nearly normal and others having great degenerative changes. Even in normal animals the cells in one group may vary in their appearance. In his studies of the effect of parathyroidectomy and cretinism on the nerve-cells of dogs,

Dye [14] met the same difficulties. He found that chromolytic reaction in nerve-cells follows the same general course in conditions of such diverse symptomatology as parathyroid tetany and cretinism, and decided that chromolysis is a reaction of nerve-cells initiated by any factor which opposes the normal physiological equilibrium of these units, a conclusion similar to that reached years ago by Van Gehuchten.[1]

In primary degenerative changes, as pointed out by Van Gehuchten [15], the Nissl bodies or chromophile particles do not, as a rule, undergo real chromolysis. When altered in this direction there is no real dissolution of the chromophile substance, but rather an achromatosis or partial disappearance or change of chromophile elements in some part of the cell. Marinesco states that, when the lesions are primary, chromolysis commences in the periphery of the nerve-cells and spreads towards the centre, whereas in secondary or traumatic degeneration the chromolysis begins centrally and spreads towards the periphery.

In the present investigations the changes in the nerve-cells can be classified among the primary or toxic group, although produced by ordinary foodstuffs without the addition of any known toxic agent. On the whole, but not absolutely, Marinesco's generalisation as to the peripheral location of changes in the Nissl bodies in primary degeneration applies to the present results, although there are some exceptions. Real chromolysis (in the sense used by Nissl) is not very common, and when present generally affects a small portion of the cell either at the periphery or near the nucleus. A few instances of chromolysis comparable to that seen in secondary degeneration were found, more especially in certain cells of the medulla. More often the granules lose their discrete form and are in a powdery or lightly staining condition, the parapyknomorphic change of Nissl. At times the Nissl bodies may be aggregated into clumps, and in other cases they may be so changed that the cell takes on a more intense, even stain and is described as chromophile.

In addition to degenerative changes in the cytoplasm, the nucleus and nucleolus are often affected. They may be swollen or shrunken. Sometimes the nucleus leaves the centre of the cell and becomes eccentrically placed. Occasionally the nucleus seems to have disappeared or its space to be invaded by the cytoplasm with Nissl bodies. At times the nucleus may appear finely granular instead of clear as it is normally.

[1] For discussions of the various hypotheses concerning chromolysis in damaged nerve cells *see* Van Gehuchten, *Anatomie du Système Nerveux, de l'homme*, 1900, Vol. 1, pp. 313-339; also S. Ramon-y-Cajal, *Histologie du Système Nerveux*, 1909, Vol. 1, pp. 214-222.

If any one of these abnormalities appeared in a group of nerve-cells the problem of description would be relatively simple, but the fact is that in any group of cells in a single animal many of these appearances can be detected in different cells. Even in the control animals, where the diet contains abundant carotene and the condition of the animals is excellent, a few of the cells will often appear abnormal. Thus it often happens that, although the observer feels fully assured that the experimental condition under investigation has produced degenerative changes in particular groups of nerve-cells, when he comes to describe these it is a matter of great difficulty.

The following brief description of changes in nerve-cells that are produced by diets high in cereals and deficient in carotene is given not so much because of any claim to finality, but rather to introduce an aspect of nerve-cell pathology which is easily producible experimentally and which, because of its probable significance in man, is worth more detailed study, for it will be generally agreed that a pathological condition of the nervous system which can be produced by ordinary foodstuffs is an important field of investigation.

The chief fixatives used for nerve-cells were 10 per cent. neutralized formol saline and Carnoy's solution (Perdrau's modification). Of these Carnoy's gave the better results owing to more rapid penetration due to the presence of acetic acid, the subsequent staining being deeper and sharper as well as more lasting.

The stains employed for demonstrating the changes seen in nerve-cells include: methylene blue (polychrome), toluidene blue and the Unna-Pappenheim stain (pyronin and methyl green). Silver impregnation methods have so far been little used in these experiments although there are indications that such methods would give interesting results.

Changes in Nerve-cells.

Dorsal root ganglia (Plate VII, figs. 1 to 7).—In the dorsal root ganglia there are normally two types of cells, the larger staining rather faintly and the smaller more strongly. The most representative change in these ganglia in carotene-deficient animals is the powdering and loss of defined granules in the main body of the cell and the apparent concentration of granules around either the nucleus or the outer edge. The only obvious differences between degenerated large and small cells is that the small cells seem to be more affected by the "piling" reaction, but this may be more apparent than real owing to their deeper staining. This "piling" of the granules around both the nucleus and the outer edge has been seen in the same cell, but it is most common to find the chromophile substance concentrated around the

nucleus. Eccentric nuclei have also been found. The nuclei of the capsule or, according to Cajal, the sub-capsule, have sometimes proliferated around degenerate cells, giving by Nissl's method a picture akin to what has been called " neuronophagia " in the cells of the central nervous system.

Gasserian ganglia.—Changes in the cells of the Gasserian ganglion are also seen in the carotene-deficient animals. These include eccentric nuclei, proliferation of the nuclei of the cell capsule, powdery granules and " piling " of the granules around the nucleus and at the outer edges of the cell, the latter being very distinct. (" Piling " appears to be less obvious in cells of the central nervous system than in those of the dorsal root and the Gasserian ganglia, which are the only cells of the peripheral nervous system so far examined).

Clarke's column and other dorsal horn cells (Plate VIII, figs. 1 and 2.)—These cells are rather small, and even in the normal the granules are not clearly defined. There are, however, undoubted differences between the animals with and without carotene. In advanced cases of carotene-deficient diets some cells seem to have disappeared, leaving only a skeleton behind, but loss of granules without other apparent change is common. In less severe cases neuronophagia, loss of definition of the granules and eccentric and slightly granular nuclei are the usual changes.

Lateral horn cells.—No striking changes have so far been noted in these cells.

Ventral horn cells (Plate VIII, figs. 3 and 4).—The large motor cells are usually entirely free from degeneration; occasionally, however, in advanced cases of vitamin A deficiency, clumping of the granules and even slight chromolysis, is found.

Nuclei gracilis and cuneatus.—The cells of these nuclei fall into line with the other cells of the afferent paths. Eccentric nuclei, powdery granules and loss of granules being seen in carotene-deficient animals, whilst in those on a carotene-containing diet they remain normal.

Lateral reticular nucleus (Plate VIII, figs. 5 and 6).—Powdering and loss of granules, clouding of the nucleus, eccentric nuclei and neuronophagia are the usual changes in the carotene-deficient animals. These groups of cells are usually only badly affected when there is much degeneration in the lateral columns of the cord and in the restiform body (see also p. 164, R. Cajal and and V. Gehuchten).

Olivary nucleus.—This nucleus receives sensory fibres from the ventral columns. Even in animals on the carotene-containing diets cells of the olivary nucleus with clearly defined granules seem to be rare. Eccentric nuclei have been found in cells of animals on a carotene-deficient diet and this seems to be the main difference from control animals.

Hypoglossal nucleus.—There are no definite differences in these nuclei between animals on carotene and carotene-deficient diets.

Nucleus solitarius (position rather more dorsal than in man).—This nucleus, which receives afferent branches from the facial, glossopharyngeal and vagus

nerves, is often severely affected. The cell changes are powdering and loss of granules, frequently with eccentric nuclei. Some of the cells in this nucleus in two or three carotene-receiving animals appear to be slightly degenerated compared with those considered as normal.

Nucleus ambiguus.—In this nucleus changes have been noted in the experimental animals. Powdering of the granules is by far the most common change, but eccentric nuclei have been seen; in a few carotene-deficient animals showing definite changes in many other nuclei no abnormalities have been seen in this group of cells. In the animals receiving carotene no degenerated cells have been found.

Vestibular nuclei (Plate VIII, figs. 7 and 8).—In carotene-deficient animals changes in the lateral and medial vestibular nuclei are seen regularly, the cells of the latter appearing most severely affected. Powdering of granules, eccentric nuclei and neuronophagia are the common changes, but in advanced cases many remnants of degenerated cells are also found. Cells of the control animals are normal.

Facial nerve nucleus (*7th*).—These cells are large and usually have well-defined nuclei and Nissl granules in both carotene and carotene-deficient animals. Degenerative changes have been found in some cells in two out of the ten facial nuclei of the deficient animals examined, but none in the carotene-fed rabbits.

Abducens and accessory 6th nuclei.—Few cells of these nuclei have been examined, but no differences between those in the animals with and without carotene have been observed. The slight changes seen in one case were within what are probably the normal limits.

Descending 5th nucleus.—Changes are usually seen in the small cells of this nucleus in the affected animals. In some advanced cases they appear to have been entirely destroyed, but powdery granules and eccentric nuclei can be found in most experiments in which the animal's diet did not contain carotene.

Oculomotor nucleus (Plate IX, figs. 1 and 2).—This nucleus, even in the control animals, contain cells which appear to be abnormal; more of these are seen in the carotene-deficient animals, and in one or two cases extensive degeneration was present.

Red nucleus (Plate IX, figs. 3 and 4).—Clumping of the granules is the most obvious change in the cells of this nucleus in the carotene-deficient animal. The granules appear larger and more widely scattered and have no definite arrangement as in the normal. Powdery granules have also been found fairly regularly, but on the other hand eccentric nuclei and neuronophagia have been so far rarely seen.

Purkinje cells (Plate VII, figs. 5 and 6).—Purkinje cells of the cerebellar cortex in rabbits receiving carotene are flask-shaped and have a large nucleus with a nucleolus situated towards the base of the flask. The protoplasm is normally granular and around the nucleus has a deeply staining demilune appearance. Of all the groups of cells examined in this work these show

perhaps the most consistent changes. In the well-established cases of carotene deficiency it is rare to see many Purkinje cells in which some change is not apparent. The nucleus becomes cloudy and can often only be recognized by means of the nucleolus, the demilune merges into the rest of the protoplasm and cannot be differentiated, the cell edges become frayed and sometimes, although the whole cell stains deeply, granules cannot be distinguished.

Dentate nucleus.—These cells in the carotene-deficient animals do not as a rule show such severe changes as the Purkinje cells, but loss of definition of the nucleus and powdery granules are often found.

Other groups of cells (Plate IX, figs. 7 and 8).—Here are included the medial accessory olivary nucleus and cells scattered in the median raphe, especially in the medulla. Many cells showing the changes described above are seen, but intense chromolytic changes such as are found when the axon of a motor cell is cut were obvious in some cells. These are the cells referred to on page 164 as exceptional in their reactions. Their appearance, in contrast with most other cells examined in this investigation, would suggest trauma of their conducting axon.

Discussion.

The foregoing account describes some of the changes in the central and peripheral nerve-fibres, and in the central and peripheral nerve-cells which can be readily produced in young rabbits by diets rich in cereals and deficient in carotene and vitamin A. Only the anatomical changes in relation to the general behaviour of the affected animals have been dealt with here. The experimental development of the study and its clinical significance I have discussed elsewhere [1 (*a*) (*b*) (*c*) (*d*) (*e*) (*f*)]. There [1 (*c*) (*d*) (*f*)] I have indicated a probable relationship between various diseases of the nervous system and diet which further work will no doubt expand. There is, for instance, good evidence that in some of the so-called toxic degenerations, especially those associated with restricted diets as convulsive ergotism, pellagra and lathyrism, a deficient intake of vitamin A and carotene is of ætiological significance. In sub-acute combined degeneration of the cord, the evidence is not so good, but it is difficult to escape the conclusion, not only that this disease is nutritional in origin, but that the responsible defect involves a biochemical mechanism in which vitamin A is concerned. Even in disseminated sclerosis there is suggestive evidence that a diet rich in vitamin A and other protective food factors increases the resistance of the nervous system to the toxic agent at fault, and that such a diet can improve the clinical condition of early acute attacks of this disease and possibly check the rate of advance in more established chronic cases.

It is necessary to emphasize that the investigations here described

and the interpretation of the results must only be regarded as of a preliminary nature; it is for neurological experts to develop the subject which is essentially one of toxic degeneration of the nervous system produced by ordinary foodstuffs and the protective effect of other specific substances. The fact that the same kind of degenerative changes can be experimentally produced by dietetic means in dogs and rats, together with the fact that morbid conditions of a comparable nature are found in man, show the subject to be one of both scientific and practical interest. The work emphasizes the importance of the specific relation of nutritional substances to the structure and proper action of the whole nervous system. Possibly the results may prove of even greater significance; the fact that degenerative changes are more easily produced in young than in old animals suggests that these same nutritional factors play a large part in determining the structural development of the nervous system, either as a whole or in part, in early life and even in the fœtus. If this is so, it is another instance of the supreme importance of the proper nutrition of the mother during pregnancy and lactation, and of the young child during the development of the nervous system.

I have already mentioned the difficulty of producing lesions in the adult animal by diet. Until recently I had not succeeded in either rabbits or dogs. Lately, however, some success in this direction has been obtained, but an account of this work I shall leave to a later publication. Suffice it to say that the intensity of the degenerative changes has not approached that described in this paper when young animals were investigated. In adult animals the amount of demyelination of fibres and the lesions in the nerve cells of the central nervous system are relatively small. There is some evidence that, apart from a deficiency of vitamin A and carotene and excess of cereal, some other nutritional defects aid in the production of degenerative lesions in the nervous system of adult animals. It would in fact appear that vitamin A bears the same kind of relation to the nervous system as vitamin D bears to bone and teeth structure. Had the experiments which led to the discovery of vitamin D been begun on adult animals, the successful issue would have been greatly delayed; for although osteomalacia in adult animals or man is clearly comparable to rickets in early life, this disease does not develop when vitamin D insufficiency is the only dietetic defect as rickets does in infants. It is possible that the difficulty of producing nerve lesions in adult animals by vitamin A or carotene deficiency is due to the fact that vitamin A controls some form of metabolism and works in conjunction with other dietetic elements in a

way comparable to the interaction of vitamin D with calcium and phosphorus. Further work will have to be done before this question is settled. It can be said with assurance, however, that the adult nervous system is much more stable under the experimental conditions employed than that of young animals and that it is more difficult to produce nervous degeneration by defective diets.

It may be asked, does this work provide any solution to the question as to whether the nerve-cell or its conducting fibre is first influenced by the special dietetic conditions used? No definite answer can be given. It was hoped that the results of experimental studies of secondary (traumatic) degeneration might throw some light on this problem. Conducting fibres when cut off from their nerve-cells degenerate, but only in certain nerve-cells does chromolysis appear. For instance, motor-cells of cerebral nerves always react in this way, while spinal anterior horn cells sometimes show chromolysis after simple section of their axis cylinders, while in other cases severer injury of their conducting fibres is necessary to produce the typical change. Again, many of the afferent nerve-cells seem to remain normal, or at least escape sufficiently great change to be demonstrated by histological methods in general use, after injury of their conducting fibres, e.g. the posterior root ganglion cells after section of the posterior roots, also the ganglion of the vagus after section of the nerve central to the ganglion (van Gehuchten [16]). Thus it would seem that nerve-fibres can in some cases be damaged without the nerve-cells undergoing obvious degenerative changes, and that this applies specially to nerve-cells and fibres of the afferent system.

Recent work of Sherrington [17] has shown on the other hand that motor nerve-cells can show changes of degeneration without their conducting fibres being structurally damaged. In his recent experiments total spinal transection in the dorsal region of the cord of monkeys produced chromolysis in a number of motor horn cells in the hind-limb region, e.g. in the 5th lumbar segment. However, the motor fibres arising from chromolysed cells which supply the tibialis anticus, the anterior longus digitans and gastrocnemius failed to show any degeneration even seventeen days after spinal transection. It is clear that nerve-cells can show chromolysis and yet their conducting fibres escape obvious myelin degeneration. It is interesting to note that, although these fibres appeared normal in structure, evidence was obtained which indicated that they were not normal in function (Sherrington [17], and Fulton and Sherrington [18]. Thus the contraction of the innervated muscle in response to a single shock stimulus was of subnormal tension value

and very sluggish as compared with the response of the same muscle in a normal animal. Sherrington calls this type of reaction " transneuronal degeneration."

So far, then, the evidence of traumatic degeneration indicates that spinal motor nerve-cells may be either normal or abnormal when the conducting fibres are degenerated, that the nerve-fibres may appear normal when their corresponding cells show chromolysis and that, in the case of some afferent nerve units, the cells may escape chromolysis when the conducting fibres are degenerating. It is evident that these results of trauma offer no aid to the solution of the problem as to whether the primary lesion in experiments described in this paper is in the nerve-cell or its conducting fibre.

At one period of the work, when the demyelination changes in nerve-fibres seemed to be the outstanding effect of vitamin-A deficiency, H. N. Green [19], working in my laboratory, endeavoured to find out whether vitamin A had some special relationship to fat metabolism. If this had been established, it might have afforded some support for the view that the nerve-fibre, and especially its myelin covering, was primarily involved in vitamin A deficiency. However, there was no evidence of any specific relationship between vitamin A and fat metabolism.

There is, as indicated above, a good deal of specificity in the nerve cells and fibres affected, the afferent system being on the whole much more liable to change than the motor system. This might be regarded as evidence that the nerve-cell lesion is primary because it seems more likely that specificity of reaction would be shown by nerve-cells than nerve-fibres. It may be possible to settle this question in the adult animal, for early observations indicate abnormality of the cell without any obvious change in its conducting fibres. Thus in one adult animal the ganglion cells of the retina are degenerating and show chromolysis while there is no obvious myelin degeneration in the optic nerve.

In their biochemical aspect these experiments have a particular interest, especially in view of earlier and contemporary work showing the close interaction between specific chemical substances and the nervous system. I refer particularly to the recent work by Dale and his colleagues [20 and 21] on acetyl choline in relation to nerve-endings and nerve-cell activity, and to the earlier investigations which established the close relationship between adrenaline and most sympathetic nerve-endings (Elliott [22]). It would appear indeed that a new stage of biochemical knowledge regarding nervous tissue is opening up, and that the time is not far distant when there will be much more information available about

the physiological action of specific chemical substances in controlling the normal structure and function of nervous tissue. It has long been known that the nervous system is specially susceptible, and gives specific responses, to many drugs of plant origin, and it might, therefore, be expected that this system would also be controlled by chemical agents with a drug-like action which are, however, physiological and present in the body. Modern investigations, including the present work, show that this is certainly the case and that the field is one of great promise.

Summary.

(1) A diet is described deficient in carotene and vitamin A which allows young rabbits to grow until abnormal movements and general behaviour indicate widespread pathological changes in the nervous system which can be demonstrated post mortem.

(2) The daily addition of 1 to 3 mgm. of pure carotene, or of some source of carotene (carrots, cabbage, &c.), to this basal diet prevents the development of these lesions of the nervous system. Vitamin A has the same protective effect.

(3) Generally speaking, it is the afferent side of the nervous system which is specially affected, but so far degenerative changes have only been found in the first and second neurons. All the afferent nerves of the head examined, including the optic nerve, the sensory fibres of the 5th, and the auditory and vestibular fibres of the 8th, suffer greatly. The motor cranial nerves usually escape, but some degeneration has occasionally been found in the 3rd nerve. In the body the same rule holds, the degeneration affecting primarily the dorsal root-fibres, those of the anterior roots remaining normal except when the nutritional deficiency has been very prolonged. No degeneration has been seen so far in the vagus nerve, even in its afferent fibres.

(4) A description of the distribution of myelin degeneration in the nerve-fibres and tracts inside the nervous system at different levels is given. Here, again, the fibres affected are mostly ascending and include the dorsal and ventral spino-cerebellar, the dorsal and ventral spino-reticulo-thalamic tracts, and the tracts of the dorsal columns. Some descending tracts suffer change, including the rubro-spinal, the dorsal longitudinal bundle and the vestibulo-spinal, all of which are associated with the mid-brain or medulla. The pyramidal tract generally escapes in the rabbit under these nutritional conditions.

(5) Degenerative changes of different degrees are seen in nerve-cells as well as in their conducting neurons; a description is given of the histological appearance of many such cells both in the central and

PLATE III.

Photomicrograph of section of high cervical cord, rabbit B, stained by hæmatoxylin after mordanting. Pale areas show complete loss of many fibres.

To illustrate paper by Edward Mellanby.

PLATE IV.

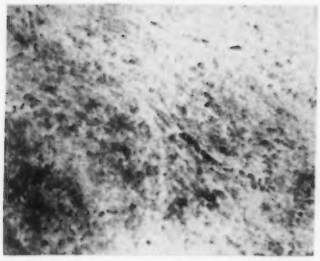

FIG. 1.

FIG. 2.

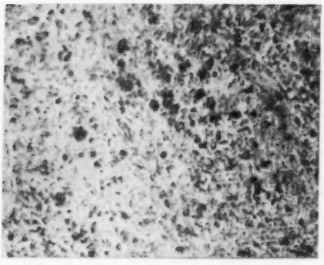

FIG. 3*a*.

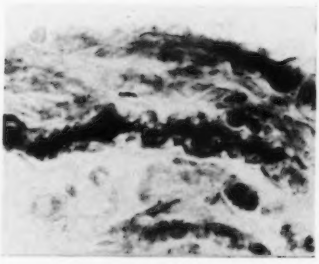

FIG. 3*b*.

FIG. 4*a*.

FIG. 4*b*.

FIG. 1.—Vestibular division of 8th nerve, diet deficient in carotene and vitamin A. Marchi stain × 280.

FIG. 2.—Vestibular division of 8th nerve, diet contained cabbage. Marchi stain × 280.

FIG. 3*a*.—Cochlear division of 8th nerve, diet deficient in carotene and vitamin A. Marchi stain × 280.

FIG. 3*b*.—Cochlear division of 8th nerve, diet deficient in carotene and vitamin A. Marchi stain × 750.

FIG. 4*a*.—Cochlear division of 8th nerve, diet contained carrot. Marchi stain × 280.

FIG. 4*b*.—Cochlear division of 8th nerve, diet contained cabbage. Marchi stain × 750.

(In this and the following plates the photomicrographs were reduced by one quarter in reproduction.)

Photomicrographs illustrating 8th nerves (vestibular and cochlear divisions) in rabbits, with and without carotene and vitamin A.

To illustrate paper by Edward Mellanby.

PLATE V.

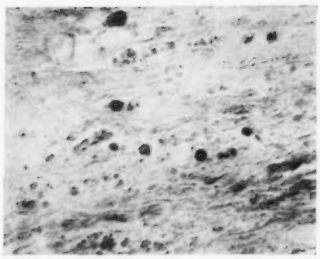

FIG. 1.

FIG. 2.

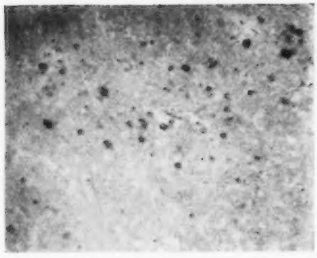

FIG. 3.

FIG. 4.

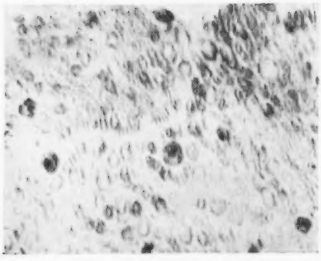

FIG. 5.

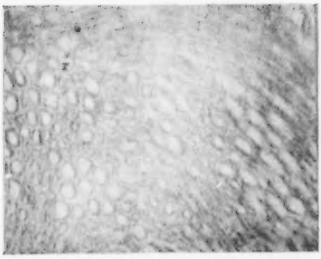

FIG. 6.

FIG. 1.—Intramedullary 8th nerve, diet deficient in carotene and vitamin A. Marchi stain × 280.

FIG. 2.—Intramedullary 8th nerve, diet contained pure carotene. Marchi stain × 280.

FIG. 3.—Optic nerve, diet deficient in carotene and vitamin A. Marchi stain × 280.

FIG. 4.—Optic nerve, diet contained carrot. Marchi stain × 280.

FIG. 5.—Sciatic nerve, diet deficient in carotene and vitamin A. Marchi stain × 280.

FIG. 6.—Sciatic nerve, diet contained cabbage. Marchi stain × 280.

Photomicrographs illustrating intramedullary 8th nerve, optic and sciatic nerves in rabbits, with and without carotene and vitamin A.

To illustrate paper by Edward Mellanby.

PLATE VI.

FIG. 1.

FIG. 2.

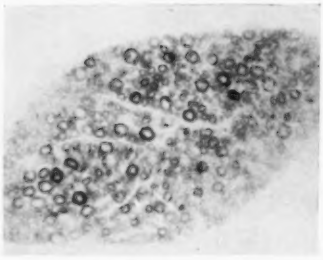

FIG. 3.

FIG. 4.

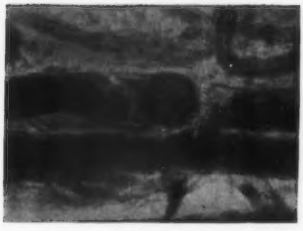

FIG. 5.

FIG. 6.

FIG. 1.—Ventral root, diet deficient in carotene and vitamin A. Normal. Marchi stain × 280.

FIG. 2.—Ventral root, diet contained cabbage and carrot. Normal. Marchi stain × 280.

FIG. 3.—Dorsal root, diet deficient in carotene and vitamin A. Annular degeneration. Marchi stain × 280.

FIG. 4.—Dorsal root, diet contained cabbage and carrot. Normal. Marchi stain × 280.

FIG. 5.—Dorsal root, diet deficient in carotene and vitamin A. Osmic method described by Cajal. × 420.

FIG. 6.—Dorsal root, diet contained vitamin A oil. Normal. Osmic method described by Cajal. × 420.

Photomicrographs illustrating ventral and dorsal roots of rabbits with and without carotene and vitamin A.

To illustrate paper by Edward Mellanby.

PLATE VII.

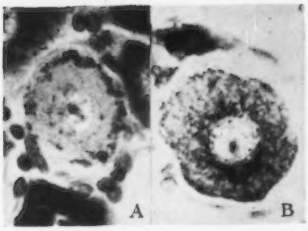

FIG. 1.

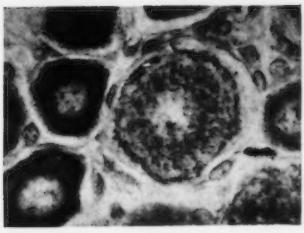

FIG. 2.

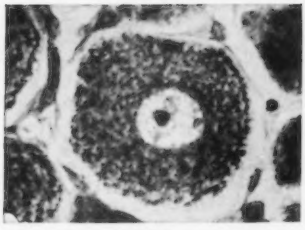

FIG. 3.

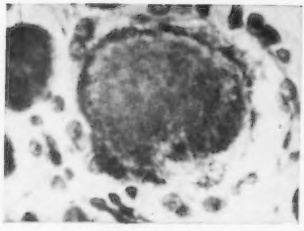

FIG. 4.

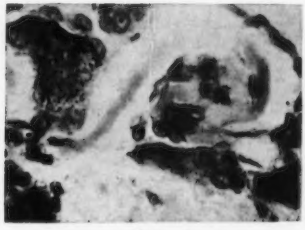

FIG. 5.

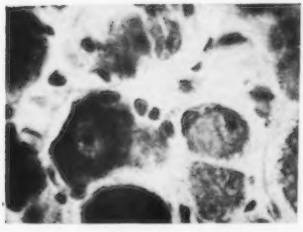

FIG. 6.

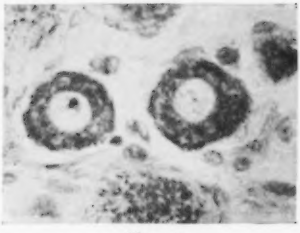

FIG. 7.

FIG. 1.—(*a*) Dorsal root ganglia × 750, large cell showing large granules around outer edge and rest of cell clear. (*b*) Dorsal root ganglia × 750, large cell showing concentration of granules around nucleus.

FIG. 2.—Dorsal root ganglia × 750, large cell showing large granules around outer edge, medium granules throughout.

FIG. 3.—Dorsal root ganglia × 750, large cell. Normal.

FIG. 4.—Dorsal root ganglia × 750, large cell with eccentric nucleus and concentration of granules around outer edge.

FIG. 5.—Dorsal root ganglia × 750, corroded cell of Cajal.

FIG. 6.—Dorsal root ganglia × 750, small cells showing eccentric nuclei.

FIG. 7.—Dorsal root ganglia × 750, small cells. Normal.

Photomicrographs illustrating dorsal root ganglia in rabbits with (figs. 3 and 7) and without carotene and vitamin A (figs. 1, 2, 4, 5 and 6).

To illustrate paper by Edward Mellanby.

PLATE VIII.

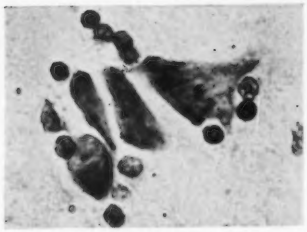

FIG. 1.

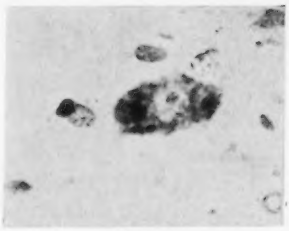

FIG. 2.

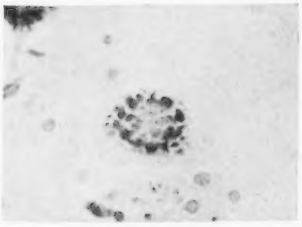

FIG. 3.

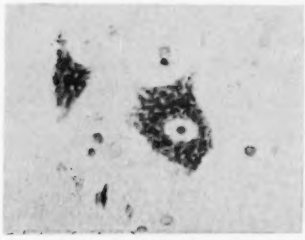

FIG. 4.

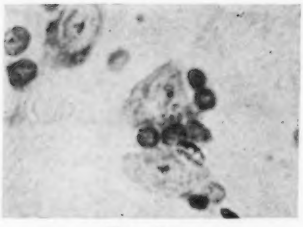

FIG. 5.

FIG. 6.

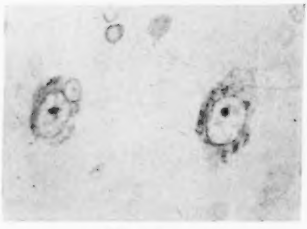

FIG. 7.

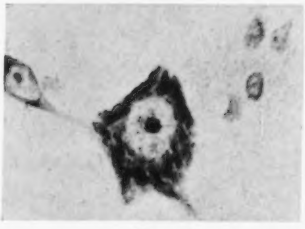

FIG. 8.

FIG. 1.—Clarke's column cells × 750, diet deficient in carotene and vitamin A. Eccentric nuclei, loss of granules and neuronophagia.

FIG. 2.—Clarke's column cells × 750, diet contained cabbage. Probably normal.

FIG. 3.—Ventral horn cells × 420, diet deficient in carotene and vitamin A. Clumping of granules.

FIG. 4.—Ventral horn cells × 420, diet contained yellow maize. Normal.

FIG. 5.—Cells of lateral reticular nucleus × 750, diet deficient in carotene and vitamin A. Loss of granules. Neuronophagia.

FIG. 6.—Cells of lateral reticular nucleus × 750, diet contained carotene. Probably normal.

FIG. 7.—Cells of mesial vestibular nucleus × 750, diet deficient in carotene and vitamin A. Loss of granules. Neuronophagia.

FIG. 8.—Cells of mesial vestibular nucleus × 750, diet contained yellow maize. Normal.

Photomicrographs illustrating cells in the central nervous system of rabbits with and without carotene and vitamin A.

To illustrate paper by Edward Mellanby.

PLATE IX.

FIG. 1.

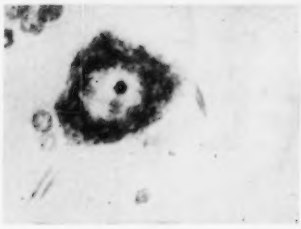

FIG. 2.

FIG. 3.

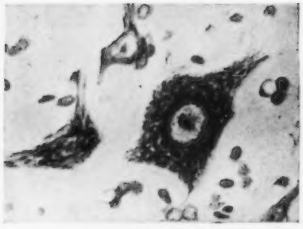

FIG. 4.

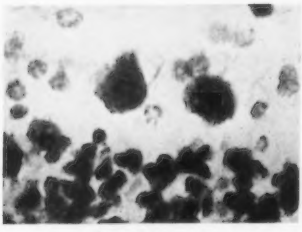

FIG. 5.

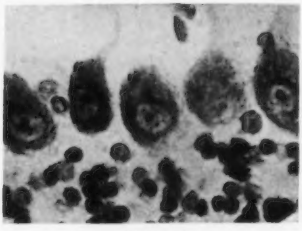

FIG. 6.

FIG. 7.

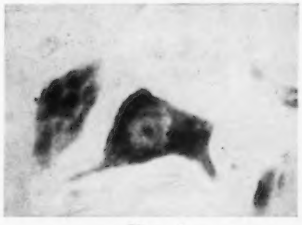

FIG. 8.

FIG. 1.—Cells of oculomotor nucleus × 750, diet deficient in carotene and vitamin A. Chromolysis and eccentric nuclei.

FIG. 2.—Cell of oculomotor nucleus × 750, diet contained carrot. Probably normal.

FIG. 3.—Cells of red nucleus × 420, diet deficient in carotene and vitamin A. Clumping of granules.

FIG. 4.—Cells of red nucleus × 420, diet contained vitamin A oil. Normal.

FIG. 5.—Purkinje cells × 750, diet deficient in carotene and vitamin A. Indefinite granules, loss of demilune and nucleus.

FIG. 6.—Purkinje cells × 750, diet contained cabbage. Normal.

FIG. 7.—Cell of medial accessory olivary nucleus × 750, diet deficient in carotene and vitamin A. Chromolysis and eccentric nuclei.

FIG. 8.—Cell of medial accessory olivary nucleus × 750, diet contained pure carotene. Normal.

Photomicrographs illustrating cells of the mid-brain and cerebellum of rabbits with and without carotene and vitamin A.

To illustrate paper by Edward Mellanby.

peripheral systems of animals receiving the carotene-deficient diet described. The groups of nerve-cells examined include those of the dorsal root and the Gasserian ganglia of the peripheral system, and the cells of Clarke's column, the Purkinje cells, those of the vestibular nucleus and many others in the central nervous system. In this case also, especially in the spinal cord, it is the afferent side which suffers most. In the mid-brain, however, the red nucleus and the dentate nucleus, and sometimes the 3rd nucleus, occasionally show some abnormalities.

I wish to express my indebtedness to my technical assistant, Mr. R. C. Stewart, for the great help he has given in this investigation, especially by improving histological methods so as to allow a large mass of material to be examined. The expenses of the work were paid by the Medical Research Council, to whom my thanks are due.

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THE EFFECTS OF LESIONS OF THE DORSAL SPINO-CEREBELLAR TRACT AND CORPUS RESTIFORME IN THE *MACACUS RHESUS* MONKEY.

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I.—Introduction.

Studies in comparative anatomy, physiology and clinical pathology have all indicated that the cerebellum as a whole tends to exert some influence which is necessary for proper co-ordination in movement. We are still at a loss for an explanation of the exact mechanisms involved. In its adult mammalian form the cerebellum is a very complex structure, including numerous afferent pathways by which influences of various types are brought to the centrally organized co-ordinated mechanisms in the cerebellum, and efferent pathways over which cerebellar influences are transmitted to reach ultimately the body musculature. For a systematic understanding of the functional organization of the cerebellum it is necessary to know not only the anatomical relationships which lay down the possibilities of physiological responses, but also the functional significance of each of the various afferent and efferent components entering into the cerebellar mechanism.

Experimental physiology has taught us a great deal concerning cerebellar function and would yield still more valuable information if experimental lesions were followed both by careful physiological observations and by careful anatomical control. The lesions should be small enough to be confined to one component, or to one combination of components, so that their effects might be systematically studied. Experiments on higher animals, as the monkey or higher primates, would be advisable. This has not been done except in a few cases. The brain of the monkey offers a cerebellum comparable to that of man, and as in this animal there are more complex types of motility of the limbs than most lower forms it is most suitable for investigations of cerebellar dysfunction.

Our aim has been to study systematically the effects of carefully controlled lesions of each of the components of the cerebellum, and it

has seemed that the point of departure would be the observation of the effects of depriving the cerebellum of its various afferent components. We have therefore taken the inferior cerebellar peduncle as a starting point, since it contains afferent components from both the spinal cord and the medulla. This paper will deal with the effects of lesions of the dorsal spino-cerebellar tract in the upper cord, and of the restiform body at various levels in the medulla oblongata where it contains in addition components from the dorsal column nuclei, from the olives and from the nucleus lateralis medullæ.

II.—Review of Literature.

Nowhere has the literature on the function of one structure been more complicated and contradictory than that on the inferior cerebellar peduncle. This would seem to be due to the complexity of the peduncle, especially at its high levels, and therefore to variability in effects according to the level of section and to the close proximity of vestibular centres. Poor anatomical controls, especially with regard to vestibular complications, have been responsible for much of the controversy on this problem. We have found that the symptoms of section of the restiform body, without involvement of neighbouring vestibular structures, differed considerably from those of lesions which also encroached upon the latter. This has convinced us of the necessity for careful microscopical control of all experimental lesions, especially when the functions of small groups of cells or fibres such as are found in the inferior cerebellar peduncle are studied.

The inferior cerebellar peduncle is usually considered as containing spino-cerebellar, dorsal-column-nuclear-cerebellar, olivo-cerebellar, lateral nucleus-cerebellar, and cranio-nuclear-cerebellar components. The exact position of each of these in different animals is very complicated. The spino-cerebellar tracts are considered as the main pathway to the cerebellum from the cord, and in our first investigation we have studied the effects of lesions of the dorsal spino-cerebellar tract in the upper cervical region. Section of these fibres within the restiform body has thrown considerable light on the result of the associated injury of other components of the peduncle.

Comparative anatomy.—According to Kappers [1], the spino-cerebellar tract in Plagiostomes is partly crossed, but is in the main an uncrossed system. It consists of two parts, a smaller corresponding to the ventral spino-cerebellar tract, and a much larger dorsal tract which joins the olivary fibres and passes to the cerebellum. The fibres end

directly in the corpus cerebelli. In the Teleosts there are likewise two systems, but the division between the dorsal and ventral portions is sharper. The dorsal spino-cerebellar tract, according to Herrick [2], is best developed in those forms in which there is a great development of cervical sensibility, as in the Triglides and Lophius. It can be followed as a distinct bundle into the cerebellum with the olivo-cerebellar fibres. In the amphibia the dorsal tract is the smaller of the two spino-cerebellar tracts, and most of its fibres end uncrossed in the cerebellum. In reptiles Kappers found essentially the same condition. In birds the two divisions of the spino-cerebellar system are again prominent. Accompanied by the olivo-cerebellar fibres, the dorsal spino-cerebellar tract enters the posterior region of the cerebellum, in which, according to Shimazono [3] and Friedlander [4], it ends predominantly in the dorso-lateral portion of the cortex. Some of its fibres are supposed to surround and even to end in the medial cerebellar nucleus.

There has been considerable controversy concerning the importance of the spino-cerebellar system in higher forms, but the consensus of opinion [5 to 46] seems to be that the dorsal spino-cerebellar tract arises chiefly from the cells of Clarke's column, that it is essentially related to the trunk and hind-limbs, that it is mainly uncrossed, and that it terminates principally in the vermis of the cerebellum. To the variations in different animal species may be due some of the differences of opinion regarding the origin, course and termination of the dorsal spino-cerebellar tract. Few authors have worked with higher forms such as the monkey, but Tooth, Mott, Grünbaum and MacNalty and Horsley all investigated the spino-cerebellar tracts in this animal. Other authors, including Löwenthal, Auerbach, Kohnstamm, Marburg, van Gehuchten, Bing, MacNalty and Horsley, and Ingvar used dogs. Cats as experimental animals were used by Auerbach, Pellizzi, Patrick, Lewandowsky, MacNalty and Horsley, Ingvar, Beck and Pass.

An interesting observation on the dorsal spino-cerebellar tract was made by Sherrington and Laslett, who by their method of " successive degenerations " showed that the tract was stratified, the outermost or more peripheral fibres coming from the lowest segments of the cord. They regarded this as an example of the law that the longer the fibres the further they lie from the grey matter, as they are displaced peripherally by the accession of subsequently entering fibres.

We cannot consider now all of the anatomical evidence for the participation of the various structures which are usually assumed to send fibres into the inferior cerebellar peduncle. Some of the authors

divide this structure into an inner and outer portion. The inner portion contains the fibres connecting the vestibular nuclei and the nuclei of the cerebellar roof. This forms the so-called I.A.K. bundle of Meynert (innere Abteilung des Kleinhirnstiel), and is essentially a vestibulo-cerebello-vestibular pathway. The outer portion of the peduncle contains the cerebellar projection of the restiform body after it has passed the level of the eighth nerve and turned upward into the cerebellum. Failure to distinguish accurately between lesions of these two portions of the inferior peduncle has undoubtedly led to much confusion, especially among the earlier authors.

The physiological observations on lesions of the restiform body and spino-cerebellar tract have, except by two or three authors, been poorly controlled histologically. The earlier authors spoke mainly of the "cerebellar peduncle" and did not confine their observations to the result of section of only the inferior cerebellar peduncle or the restiform body. In fact, they did not even differentiate the many components of the large mass of fibres connecting the medulla and pons with the cerebellum, and spoke of the whole mass of what we now know as the superior, middle and inferior peduncles as a single large peduncle.

Serres [47] and Magendie [48] were apparently the first to experiment on the cerebellar peduncles. In unilateral lesions they found that the most constant symptom was torsion movements of the animals around the longitudinal axis to the side of the injured peduncle. The lesions apparently involved all three peduncles. Other authors, as Longet [49], Lafargue [50], and Lussana [51], always found torsion movements toward the side opposite to that of the lesion. Claude-Bernard [52] observed torsion movements toward the side of the injured peduncle when the lesions were caudal to the exit of the fifth nerve. On the other hand, section of the peduncle anterior to the fifth nerve was accompanied by torsion movements towards the opposite side.

Ferrier [53] and Hitzig [54] confirmed in general the findings of Serres and Magendie. Ferrier explained the contradictory reports of previous authors as due to a simple misunderstanding and dependent on whether one looked at the animal from in front or from behind. However, even after Ferrier's explanation, authors differed widely in their descriptions.

Ferrier and Turner (1894) [55] described in detail the symptoms of section of the various cerebellar peduncles in monkeys. In animals in which the left inferior peduncle was cut there was a curving of the vertebral axis to the left, with flexion of the left limbs and extension of

the right. Every attempt at movement produced rolling movements from the right to the left, and the animal held on tightly to any means of support. Slightly later they observed tilting of the chin to the right. The falling and rolling movements persisted until the ninth day, and nystagmoid movements were observed. Histological examination revealed that the nucleus cuneatus was involved to some extent and that the restiform body was destroyed just before it bends into the cerebellum. The authors described a characteristeric attitude after section of the inferior peduncle, consisting of curvature of the vertebral axis with its convexity towards the side of the lesion, adduction and flexion on the side of the lesion, and abduction and extension of the opposite limbs. In the majority of the cases the chin deviated to the opposite side.

Biedl, in 1894 [56], reported one case of section of the restiform body in a cat. He found a typical group of symptoms including rolling movements and disorders of motility in the extremities of the operated side, disturbance of co-ordination in the legs and head, and rolling movements toward the opposite side whenever the animal made any effort to move. The author did not present an anatomical description of this lesion, except to say that the descending trigeminal root was involved.

Mott, in his extensive studies of the afferent tracts in the monkey, gave no description of the behaviour of his animals.

So far as sharply circumscribed lesions of components of the inferior cerebellar peduncle were concerned the first work was done by Marburg and Bing. Marburg (1904) divided the dorsal spino-cerebellar tract in dogs, usually on one side at or above the second cervical segment. Two days after the operation the head movements were normal. The ipsilateral fore-limbs were turned outwards, the hind-limbs were in maximal abduction. The pelvis was rotated to the operated side and the vertebral axis was usually concave towards this side. All of these symptoms, except abduction of the hind-limb, were inconstant. The animal usually supported itself on the healthy side. The posterior limbs were usually more closely approximated to the anterior limbs than in a normal animal. There was no deviation toward the healthy side on walking. The animal showed marked uncertainty on climbing stairs. While sitting still very little abnormal was noted except that some animals occasionally rested with the dorsum of the foot downward, suggesting a loss of sensory reflexes. The animals reacted normally to pin-prick. There was no change in muscle tone or in the tendon

reflexes. The animals recovered quickly, and after two weeks it was difficult to tell the side of the operation, though a slight abduction of the ipsilateral hind-leg usually persisted.

After bilateral section the dog usually showed definitely postural defects with outward rotation of the feet, maximal adduction of the fore-limbs and abduction of the hind-limbs. The fore-limbs were often crossed. The involvement was much more marked in the hind-limbs. There was marked lateral swaying resembling that of a drunken animal. The disability was greater in complicated actions as climbing stairs. The animal was unable to raise its leg upward while its fore-paw rested on the upper step. There was always some unilateral "paresis" shown by abnormal postures of the feet which the animal did not correct; this condition was only present in the "paretic" limb, and it always ran parallel to the paresis. Sensation and the tendon reflexes were normal. In all these dogs there was degeneration not only of the dorsal spino-cerebellar tract but also of the descending pyramidal tract. It is therefore difficult to evaluate the rôle played by this pyramidal deficiency.

Bing (1906) published an extensive monograph on the significance of the spino-cerebellar system and reported the findings associated with lesions of it. He attributed most of the disability to special forms of disturbance of regulation of the muscles and to a diminution of muscle tonus. To these were due the abnormal postures and movements which were greater in the pelvis and shoulder-girdle musculature. Thus the so-called "principal movements" of Munk, which are supposed to be related to subcortical activity, were chiefly affected. Bending of the trunk to one side would appear to be due to this type of disturbance. Bing also attributed inability to turn toward one side to loss of general basic movements. He noted that the disturbance in the principal movements was more marked in the posterior extremities than in the anterior. The hypotonia was more pronounced in the muscles of the pelvis and shoulder girdles. In the acute stage the ipsilateral limbs were abducted and were used only very slightly for support, the weight being shifted on to the normal side. There was no stumbling or falling. There was also a failure to correct abnormal postures of the limbs. The pelvis was rotated towards the operated side; the vertebral column was normal. The animals appeared normal in sitting and lying postures. The limbs were more adducted in walking, and at times were even crossed. The hind-leg of the operated side was often placed too far forward. The involved limbs showed slight shakiness and ataxia.

There was usually no deviation to one side on walking, but occasionally the animals walked in circles toward the healthy side and presented a considerable difficulty in turning towards the operated side. There was no spontaneous dorsi-placing of the feet. The ataxia was more marked when the animal was blindfolded and in jumping the animal often fell toward the operated side. Tarsal and carpal tone was essentially normal. Sensation and the deep reflexes were undisturbed likewise. Improvement proceeded rapidly, and by the fourth day the abduction was considerably less, muscle tone was approximately normal, and the animal rarely fell.

After four weeks the only difficulty was in turning towards the operated side in search of food. As the author illustrates his anatomical descriptions only by schematic drawings it is difficult to make out the exact extent of the lesions.

Bing disagreed with some of Marburg's findings particularly as pyramidal lesions had complicated the latter's observations. According to Bing the symptoms were due to involvement of reflex paths resulting in a deficiency of afferent stimuli to the cerebellum, for only afferent pathways were cut in his experiments. The symptoms resembled in part those due to sections of the dorsal roots, and he referred to the similarity of the pseudo-paraplegic state of Munk and Bichel, in which animals subjected to centripetal lesions showed ataxic postures. Bing believed that the dorsal spino-cerebellar tract has a bilateral origin. He could not determine exactly the reflex pathway involved, but suggested it was possibly "peripheral sensory neuron to dorsal spino-cerebellar tract, to vermis, to the tractus cerebello-tegmentalis, to the red nucleus, to the rubrospinal tract, to the peripheral motor neuron." He referred to the remarkable constancy of this neuron chain in the animal series; it has been described even in the Selachians.

Bing found no disturbance of cutaneous sensation but considered it possible that the spino-cerebellar tract subserves deep sensibility, and that lesions of this system may therefore disturb muscle tone. Compensation occurs through the cortical, subcortical and spinal pathways. That the fore-limbs were less involved than the hind-limbs in cervical lesions, he considered possibly due to the greater participation of the psychomotor cortex in movements of the arms or fore-limbs. The more severe affection of the hind-limbs may be explained by the distribution of Clarke's column which extends from the lower portion of the cord to the upper dorsal segments.

Bing and Marburg are the only authors who have described at

length isolated lesions of the spino-cerebellar or restiform body systems, but brief descriptions have been given by other authors. For instance, Bruce and Schäfer (1910), in studying spinal degeneration in monkeys, mentioned that no permanent symptoms followed lesions of the dorsal spino-cerebellar tract in the upper part of the cord, and that the animal showed very little abnormality in the acute stage.

Bechterew (1908) [57] has also referred to the effects of lesions of the inferior cerebellar peduncles. In dogs he made lesions either below or above the entrance of the eighth nerve. In the animal in which the left inferior peduncle was cut caudal to the entrance of the eighth nerve the head and trunk were rotated around the long axis of the body toward the side of the lesion, with concomitant deviation of the eyes in a diagonal direction and nystagmus. The animal assumed a forced posture lying on its left side, with the ipsilateral limbs flexed and the contralateral extended. In the animal in which the peduncle was cut above the point of entrance of the eighth nerve, there was also turning of the head and trunk toward the operated side with marked deviation of the eyes and nystagmus. The torsion movements around the long axis persisted. The animal always lay on the ipsilateral side with the contralateral limbs extended. Bechterew believed that the effects of the lesions were the same whether the peduncle was cut above or below the entrance of the eighth nerve. He considered that the involvement of the centripetal paths from the spinal cord and the labyrinths to the cerebellum by way of the inferior peduncle was chiefly responsible for the torsion movements around the long axis of the body.

From this summary of the literature it may be seen that little has been done, especially in higher animals such as the monkey, to correlate controlled anatomical lesions and behaviour of the animal. Most of the investigations on the anatomy of the spino-cerebellar tracts or the various peduncles included practically nothing on the behaviour of the animals, while in most publications in which the symptoms are carefully described the anatomical descriptions are poor. And apart from the work of Mott, Bruce, Ferrier and Turner, there are no observations on monkeys. We therefore felt that there is still an opportunity for systematic investigation to be carried out on carefully controlled experimental lines. We adopted the plan of producing lesions limited as far as possible to each of the components of the inferior cerebellar peduncle. Each experiment has been carefully controlled by anatomical serial sections.

III.—Personal Observations.

Experimental technique.—The operations were all performed on *Macacus rhesus* monkeys. Lesions were made at three levels. In the first the dorsal spino-cerebellar tract was divided in the upper cervical region, usually at about C-4 or C-3. The second level was above the caudal origin of the restiform body at about the lower or middle level of the nucleus cuneatus. The third level was higher in the restiform body, just caudal to the entrance of the eighth nerve.

The spinal lesions were made in a very simple manner. After laminectomy the dura was opened and a dorsal root was mobilized just below its point of entrance. A small superficial lesion was made just lateral to the line of separation of the dorsal columns and lateral columns. Usually this could be accomplished with little bleeding. Most of the lesions were made with a small sharp scalpel or a Darling capsulotomy knife, but in a few cases a small curved cautery was used. The dura was usually not sutured so as to avoid any pressure. Occasionally one dorsal root was cut in order to expose the dorsal spino-cerebellar tract more clearly. To produce lesions in the restiform body a suboccipital approach was made to the cerebellum. After the bone had been removed up to the transverse sinuses the dura was opened exposing the postero-inferior surface of the cerebellum. The vermis and medial portion of the lateral lobe were retracted upwards and it was then possible to see clearly the vestibular eminence, the medulla lateral to this, and the eighth nerve curling around the upper lateral surface of the medulla. The lesions were produced by small sharp hooks. The usual sub-occipital closure was performed without suturing the dura. In all cases the animals usually made remarkably rapid recoveries from the ether anæsthesia. One hour after operation they were usually moving around in the cage and attempting to eat. Careful observations of the general behaviour and of the neurological disturbances were made on all animals three hours and twenty-four hours after the operation, and at the latter period moving pictures were taken. The animals were then observed carefully until the time of sacrifice.

Serial sections were made of all brains. They were studied by Nissl's cell stain, the Weigert myelin-sheath stain, and the Marchi method.

In all twenty-two animals were operated on for this series of observations. We shall present here a typical protocol from each of the characteristic lesions at different levels.

Protocol No. 1, *Cer.* 119.

August 1, 1933. *Operation*: *Section of left dorsal spino-cerebellar tract at the fourth cervical segment.*—A small superficial lesion was made at the level of entry of the left fourth cervical root. Before making the lesion in the cord the fourth left dorsal root was cut in order to be able to expose clearly the lateral surface of the cord. There was no bleeding or visible swelling of the cord.

Three hours after operation.—While coming out of the anæsthesia, the animal has shown no asymmetry of posture. When recovered from the anæsthesia the most marked symptoms are an apparent left-sided weakness associated with ataxia and falling toward the left. There are slight hypotonia and diminution of the reflexes on the left. The right side appears normal. The grip of the left limbs is strong, contrasting sharply with its absence in lesions of the dorsal columns at the same level. There is a left-sided diminution in the placing and hopping reflexes. The ataxia, falling and weakness manifest themselves especially when the animal tries to walk, climb or reach for food. In sitting still there may be at times an increased abduction in the left hind-limb, but no abnormality of posture in the left fore-limb. In walking the left limbs show a dysmetria with occasional excessive lifting or falling and unsteadiness, without, however, any definite dragging of the limbs such as occurs when the pyramidal tract is involved. The animal falls occasionally to the left. When climbing the animal uses both sides of the body fairly well, but the left limbs show a slight lack of steadiness. All the fingers are employed and the grip is firm and secure. The left deep reflexes are diminished as compared with the right. The muscle tone on the left, as tested by resistance to passive movements, is also reduced. The responses to touch, pin-prick, deep pressure and change in position of the limbs seem normal on both sides of the body. There is no evidence of involvement of any of the cranial nerves. The deficiencies at this time were definitely much less disabling than those due to lesions of the dorsal columns. The disability manifests itself chiefly as a sort of dysmetria. This is shown by the occasional missing of an object for which the animal reaches. There is, however, no intention tremor.

September 1, 1933: *Twenty-four hours after operation.*—The general condition of the animal is excellent. There is little abnormal except slight weakness, hypotonia, inco-ordination of movement and diminution of the reflexes in the left limbs, but even these symptoms do not appear to be as marked as they were. The animal no longer falls towards the left, except occasionally when it jumps or runs very fast, then it may stumble slightly towards the left. The symptoms are as marked in the fore-limbs as in the hind-limbs. Vestibular testing reveals normal responses on both sides. The labyrinthine reflexes are undisturbed. The placing and hopping reflexes on the left have recovered to some extent.

September 11, 1933: *Eleven days after operation.*—At this stage it would be difficult to distinguish the animal from a normal monkey, but there are still slight disabilities on the left, such as a tendency to abduction of the left

limbs and a slight lack of elasticity in them on landing from a jump. The deep reflexes are also slightly less active on the left. The animal no longer falls to one side and the sensory responses appear normal. The grip is strong and there is no longer any dysmetria.

The animal was killed on this day for study of its nervous system by Marchi's method. The lesion lay directly in front of the fourth dorsal cervical root which had been divided in the operation.

Anatomical Study.

Microscopically the lesion appeared to be confined to the region of the left dorsal spino-cerebellar tract at the level of the fourth cervical segment. The left fourth cervical dorsal root had been cut and its degeneration could be clearly followed into the dorsal columns and upward to the nucleus cuneatus and the nucleus of Clarke-Monakow (nucleus cuneatus externus). Sections of the cord below the lesion revealed no degeneration in the left pyramidal tract.

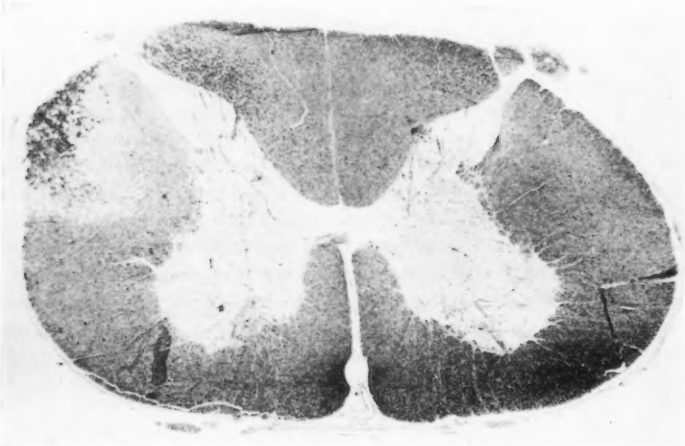

FIG. 1.—Section of the cervical spinal cord at the level of the maximum extent of the lesion, showing the slight paling in the region of the pyramidal tract, which, however, has not produced descending degeneration. The incoming degenerated fourth cervical root, which was cut in the operation, can be clearly seen. Marchi preparation.

Fig. 1 shows a section of the cord at the level of the lesion which is confined to the region of the dorsal spino-cerebellar tract, but there is slight rarefaction in the region of the pyramidal tract. The degenerating fourth cervical root can be seen entering the dorsal column area.

Fig. 2 shows the degenerating fibres just before they pass around the tubercle of Rolando to enter the restiform body. The degenerating fibres from the sectioned fourth cervical root can be seen in the funiculus cuneatus. At higher levels the degeneration can be easily followed in the restiform body,

in which the fibres take up a lateral but fairly diffuse position, in perhaps the lateral two-thirds of the restiform body. The medial third is occupied by the entering olivary and dorsal column nuclear fibres, particularly fibres from the nucleus cuneatus externus (Clarke-Monakow). The degeneration can be followed cephalad well up into the lateral portion of the inferior cerebellar peduncle and into the vermis. The exact termination of the tract has not been determined.

FIG. 2.—Section of the lower medulla at the level of the pyramidal decussation, showing the large group of degenerated fibres of the left dorso-spinocerebellar tract just before they pass around the tubercle of Rolando to form the restiform body. The degenerated fibres of the cervical root in the dorsal columns can be seen on their way to the nucleus of Burdach and the nucleus of Clarke-Monakow. Marchi preparation.

Protocol No. 2, Cer. 23.

July 14, 1932. *Operation: Lesion of the right restiform body.*—The floor of the fourth ventricle was exposed by upward retraction of the vermis. At a point where the restiform body runs laterally and at a level of about the middle third of the nucleus cuneatus an incision was made through the restiform body by a fine hook. At the end of the operation the animal was in fine condition. No spontaneous nystagmus was observed.

Three hours after operation.—With the animal well out of anæsthesia the principal manifestation is a weakness in the right limbs and a tendency to fall towards the right side. When the animal attempts to walk its right limbs either slip away on the floor, or crumble and the animal falls towards the right. No involvement of the cranial nerves is observed. The pupils are equal and react well to light. The extra-ocular movements appear normal. The sensory fifth and the biting muscles appear unaffected. There is no facial paralysis and the animal apparently hears well in both ears. No abnormality

is noticeable in the position of the head. The chief symptom is an apparent weakness of the right limbs. The tone of the right limbs is much diminished as compared with the normal left limbs. The grip of the limbs is, however, good. The left side of the body appears absolutely normal. When the animal is suspended by the tail with the head downward and the eyes open a normal symmetrical dorsiflexed position of the head is observed. The right limbs are slightly more flexed than the left, which are in the normal semi-flexed position. When the animal is held in the right or left lateral positions with eyes open, positions of the head are normal. The falling reaction is normal. The animal jumps in a straight line, but it lands very heavily on the right side. There are occasionally fine jerky tremors in the right limbs and some evidence of dysmetria in the right fore-limb, for when the animal reaches for a peanut it is apt to miss and fall short of the object at first, but it gradually creeps up so as to grasp it. The deep reflexes on the right side appear slightly diminished. Sensory examinations show no gross disturbance. In this acute stage the symptoms are similar in type but more definite than those due to a lesion of one dorsal spino-cerebellar tract.

July 15, 1932: *Twenty-four hours after operation.*—The general condition of the animal is essentially the same as at the three-hours' stage, but it no longer falls toward the right side. This now occurs only when the animal attempts to run fast or make a sudden turn, when there may be slight slipping out or giving way of the right limbs. Otherwise the animal gets about fairly well. A slight fine tremor and some dysmetria are still present in the right limbs. The grasp is well maintained. Rotation and caloric tests give normal nystagmus responses in both directions and on both sides. The postural, falling, and righting reflexes are normal.

July 16, 1932: *Forty-eight hours after operation.*—The general condition of the animal is unchanged, and it seems to be improving rapidly. It runs pretty well with a slight tendency to ataxia and some hypotonia of the right limbs; when it jumps there is a tendency to land rather more heavily on the right side, and occasionally these limbs slip out. No rotation of the head.

July 21, 1932: *One week after operation.*—The animal now runs pretty well. Save for slight weakness, a tendency to abduction of the right fore-limb, weakness or lack of spring as manifested by heavy landing in jumping and occasionally stumbling when it runs fast, little can be seen which is definitely pathological on either side. There is no evidence of any definite paresis. The reflexes and tone of the right limbs now appear to be normal. Rotation and caloric stimulation give normal responses on both sides. The postural, falling and righting reflexes again give normal responses.

July 28, 1932: *Two weeks after operation.*—Condition essentially the same as at the one-week stage.

August 14, 1932: *One month after operation.*—The general condition is excellent. There are practically no abnormalities except, perhaps, slight weakness of the right side which is seen only when the animal jumps from a high place. There is a slight tendency when the animal jumps to fling the

right limbs slightly higher than the left and to stumble very slightly when it lands, but even this is not definite.

September 14, 1932: *Two months after operation.*—The condition is essentially the same as at the one-month stage.

October 14, 1932: *Three months after operation.*—The general condition of the animal is excellent. It now jumps as a normal animal. Little can be seen that might be definitely interpreted as abnormal.

Anatomical Study.

The lesion is confined to the right side and is at the level of the junction of the lower and middle thirds of the right nucleus cuneatus. It involves the brain-stem near the dorsolateral border of the nucleus cuneatus, and passes downward and laterally to just below the inferior border of the restiform body. Fig. 3 shows the lesion at its greatest extent.

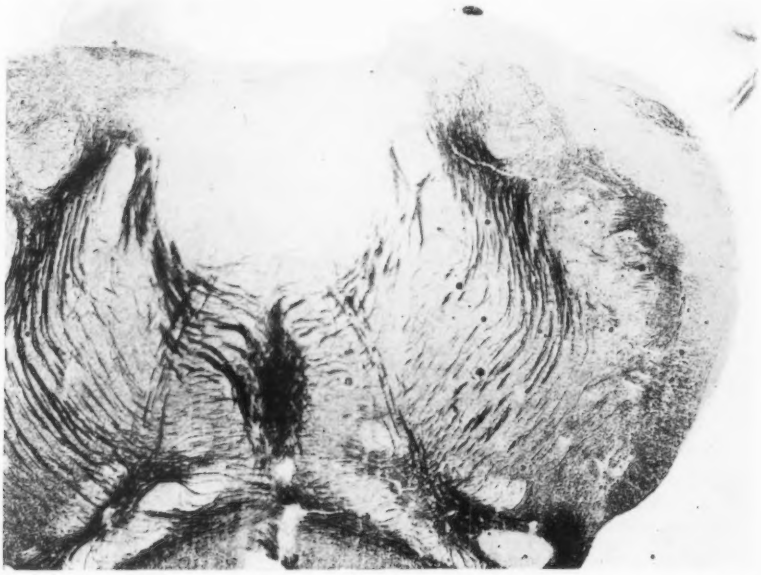

FIG. 3.—Section of the medulla at the level of the maximum extent of the lesion of the right restiform body, showing the direct involvement of the restiform body on the right. The nuclei of Goll and Burdach are not involved to any great extent in the lesion. The few peripheral fibres which are apparently spared at this level, are included in the lesion a section or two higher. Weigert preparation.

The structures involved are the most dorsolateral tip of the nucleus cuneatus, the restiform body, the descending root of the fifth nerve and part of the nucleus of its descending root. Below the lesion in the first or second cervical segments a degeneration is clearly seen in the right descending root of

the trigeminus. At the level of the lesion, where the internal arcuate fibres are being formed, there is a slight diminution in these fibres on the right side as compared with the normal left side. The right nucleus cuneatus externus (Clarke-Monakow) is involved in the lesion. At higher levels there is a marked degeneration in the right corpus restiforme, especially in its lateral two-thirds (fig. 4). Still higher the medial border of the corpus restiforme retains a considerable number of relatively normal fibres; these come from the olive. At the level of the trapezoid decussation there is slight paling of the middle portion of the left lemniscus, due undoubtedly to involvement of a

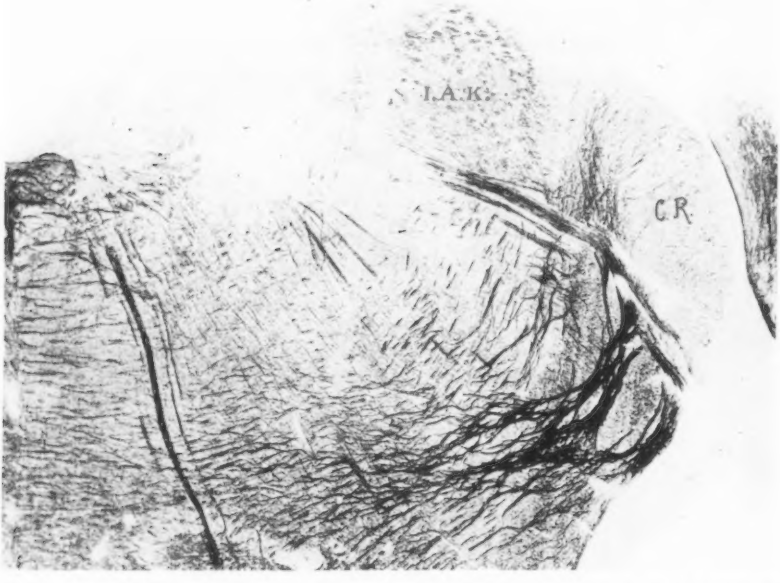

FIG. 4.—Section of the medulla at a higher level than that of fig. 3, at the zone of entrance of the eighth nerve. The restiform body on the right is seen to be degenerated and the incoming olivary fibres are seen to be adding themselves to the restiform body on the medial aspect. There is no evidence of degeneration involving the I.A.K. bundle. Weigert preparation C.R. = corpus restiforme.

few of the fibres from the right nucleus of Burdach. The degeneration in the restiform body can be followed upwards to the vermis. The lesion therefore involved all the fibres of the spino-cerebellar tract, a majority of the fibres from the ipsilateral nucleus of Clarke-Monakow (external cuneate nucleus) and probably some, if not most, of the fibres from the ipsilateral nucleus lateralis medullæ. The extent of the lesion accounts for the greater severity of the clinical manifestations in this case as compared with those of the previous case in which the fibres of the dorsal spino-cerebellar tract only were involved.

Protocol No. 3, *Cer.* 142.

Operation, January 2, 1934: *Section of the right restiform body just below its passage under the eighth nerve.*—The cerebellum was retracted and a small superficial lesion was made in the right restiform body just before it disappeared under the eighth nerve. Very little bleeding occurred.

Three hours after operation.—While the animal was coming out of anæsthesia there was no asymmetry of posture. Whenever the animal attempted to stand, however, it fell to the right side. There has been no spontaneous nystagmus. When the animal had fully recovered from the anæsthetic the symptoms closely resembled those seen in Protocol No. 2, where the lesion of the right restiform body was at a lower level. In the present case, however, the symptoms appear to be more marked and there is a greater tendency to fall to the right. When it attempts to stand it falls over towards the right, perhaps two out of three times. The other disturbances include some ipsilateral hypotonia, depression of reflexes, ataxia, dysmetria and diminution of the placing and hopping reflexes. The animal grasps objects spontaneously in a perfectly normal manner, except for the dysmetria. There are no tremors at rest, no intention tremor, no spontaneous shaking movements and no spontaneous nystagmus. The vestibular reflexes are normal. Sensation, so far as can be determined, is also normal. There are no signs such as rolling movements, asymmetry or nystagmus to indicate the probability of any vestibular complication. When the animal sits it presents abducted postures of the right limbs. It uses the right limbs in reaching for food and grasps a stick or the cage apparently normally.

January 3, 1934: *Twenty-four hours after operation.*—The main symptoms are identical with those found at the three-hours' stage, but the animal does not fall so often to the right side. When it jumps it lands heavily on the right limbs, which tend to sprawl out. This is slightly more pronounced than in animal No. 2. There is no tendency toward rotation of the trunk while it is in the air. When swimming its attitude is symmetrical, and apparently it has normal control over its limbs. Tests reveal no evidence of involvement of the vestibular system, normal responses being obtained from both sides.

January 4, 1934: *Forty-eight hours after operation.*—The condition is essentially the same, the main difference is that the animal can jump somewhat better and avoid falling more easily. No new symptoms have appeared and the stability of the animal seems improved.

January 9, 1934: *One week after operation.*—During the past week the animal has improved considerably. It rarely falls now and only when it makes a sudden movement towards the right side. Muscle tone is still somewhat diminished in the right limbs, and the knee-jerk is still depressed on this side. There has been no evidence of any vestibular complication. The limbs are used well spontaneously, but the animal occasionally misses objects. There has been no asymmetry in posture and no shaking or forced movements of any type. It jumps fairly well and manifests some lack of strength and springiness in the right limbs only when it lands from a long or high jump.

January 14, 1934: *Twelve days after operation.*—During the past three or four days the animal has improved considerably. It now runs very well, using both sides of the body normally. There is still no evidence of any vestibular complication, but the tone of the muscles and the reflexes are diminished on the right, and there are indications of lack of strength and of spring on this side in jumping.

It was killed on this date and studied with the Marchi method to determine the extent of the lesion.

FIG. 5.—Section of the medulla at the zone of entrance of the eighth nerve. The marked degeneration of the right restiform body can be seen. The I.A.K. bundle shows no degeneration. Marchi preparation.

Anatomical Study.

The Marchi preparations are extraordinarily clear. The lesion, which can be clearly delineated, includes the right restiform body in its entire extent at a level about 1 to 2 mm. caudal to the entrance of the eighth nerve. The lesion does not involve the area of the I.A.K. bundle, but is sharply limited to the restiform body itself. In sections below the lesion there is no degeneration in the descending fifth root. Fig. 5 shows a section of the medulla at the entrance of the eighth nerve. Here there is practically complete degeneration of the right restiform body. It can be seen that there is no involvement of

the eighth nerve or of the I.A.K. bundle. Fig. 6 comes from a higher level where the inferior peduncle is bending upwards into the cerebellum. A large group of degenerated fibres from the right restiform body can be seen entering the vermis. The lesion involves all the fibres from the spino-cerebellar tract, those from the ipsilateral nucleus lateralis, those from the ipsilateral external cuneate nucleus and a majority of the fibres from the opposite inferior olive.

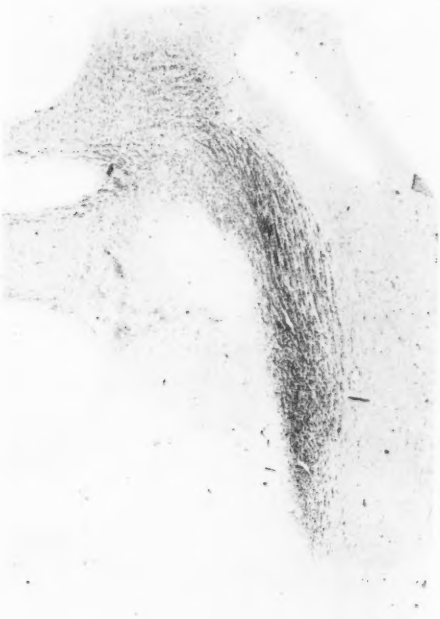

FIG. 6.—Section of the medulla and cerebellum at a level where the inferior peduncle passes dorsally into the cerebellum. The large group of degenerated restiform body fibres can be seen passing dorsally to enter the vermis. Marchi preparation.

Protocol No. 4, Cer. 28.

July 14, 1932. *Operation: Lesion of both inferior cerebellar peduncles.*—The fourth ventricle was opened with the vermis retracted upwards, the inferior peduncles just lateral to the vestibular eminence were exposed and a lesion was made with a small hook on each side. Immediately after the lesion, while the animal was still under the anæsthetic, its general condition was good. No peculiarities of posture were observed.

Three hours after operation.—The animal is fully recovered from the anæsthetic; it tends to hug the wall of the cage closely. It occasionally

sways from side to side and jerky movements of the limbs sometimes occur. The head is slightly flexed on the chest. When the animal is placed on the floor it tends to extend suddenly all four limbs and to fall flat on the floor banging its head. This may occur suddenly and spasmodically even in an attempt to walk, or the anterior limbs may flex so that the animal suddenly falls on its chest and head. There is no spontaneous nystagmus to indicate any vestibular lesion. All the labyrinthine reflexes appear normal. The deep reflexes are diminished on both sides.

FIG. 7.—Section of the medulla at approximately the maximum point of the bilateral lesion. The lesions are seen to involve both restiform bodies in their entirety. Weigert preparation.

July 15, 1932: *Twenty-four hours after operation.*—The symptoms are unchanged. The animal is still unsteady, walks with a wide base and may fall on its head and chest to the floor. In reaching for food there is definite bilateral ataxia or dysmetria, but no intention tremor. In running across the top of the cage or on the floor it may be unable to stop and plunges headlong into the wall. When the animal is placed on the floor it tends to spring about madly and appears to have no control. It cannot jump toward the cage. When it tries to jump forwards it may leap straight up in the air and land on its back or turn over in all sorts of queer ways, and every once in a while there is a tendency towards forced falling with all limbs extended. The deep reflexes and muscle tone appear diminished throughout. This inability to

control the body in motion appears to be due to a lack of control of the limbs rather than to an inability to orient the body or head in space as is found in vestibular animals. When the monkey is held in the air it makes vigorous and mainly successful efforts to right itself. It can swim normally under water. Vestibular tests reveal no disturbances.

July 17, 1932: *Three days after operation.*—The condition of the animal remains the same, but now when it is placed on the floor it does not stumble so wildly. It prefers to lie flat or to walk about slowly.

FIG. 8.—Section of the medulla at the level where the restiform bodies bend upward into the cerebellum. The degeneration in both restiform bodies can be clearly seen. The I.A.K. bundles are seen to be well preserved on both sides. Weigert preparation.

July 21, 1932: *One week after operation.*—The condition of the animal is excellent. It appears perfectly at home in the cage, although it manifests a very marked fear reaction. On the floor it still shows a tendency to fall suddenly, and in running there is still undue flexion of the fore-limbs with drooping of the chest and head toward the floor. The ataxia and dysmetria are still present. The deep reflexes and muscle tone now appear about normal throughout.

July 28, 1932: *Two weeks after operation.*—The condition of the animal is essentially the same.

August 3, 1932: *Three weeks after operation.*—It is in much the same state, but it now gets about rapidly on the floor with only slight signs of inco-ordination and lack of control.

August 14, 1932: *One month after operation.*—There are practically no abnormalities except a tendency when jumping to land heavily on the floor and perhaps to extend all four limbs slightly more than the normal monkey while jumping. The deep reflexes and muscle tone appear normal throughout. The functions of the cranial nerves are unaffected. No tremors or abnormal movements of any type occur in the limbs and there is no ataxia or dysmetria. The falling, position and righting reflexes are normal. Sensory examination and the vestibular tests reveal no disturbances. The animal, however, does

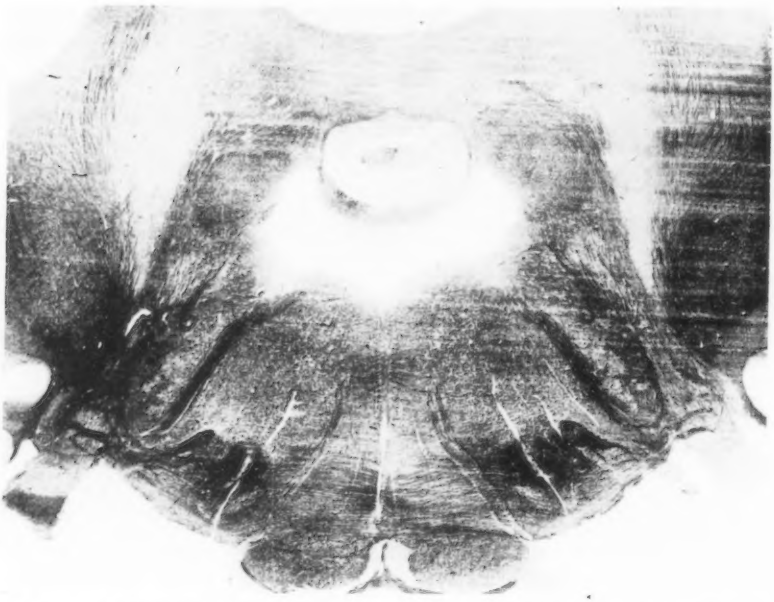

FIG. 9.—Section of the medulla at a higher level than that of fig. 8, showing the fibres from the restiform bodies of both sides radiating dorsally into the vermis. Weigert preparation.

not seem to get about very well on the swinging bar and occasionally falls from it. Otherwise it seems sure-footed and climbs quickly and well.

September 14, 1932: *Two months after operation.*—There is no change; it is practically a normal monkey.

Anatomical Study.

The lesions involve the restiform bodies near the junctions of the middle and upper thirds of the nuclei cuneati. Weigert preparations of the brain-stem in serial section reveal that the right-sided lesion is slightly higher; it extends

from the angle between the upper outer part of the nuclei cuneati and the restiform body and passes downward and laterally to destroy the restiform body. Fig 7 shows the lesions in their greatest extent. On the left a small part of the inferior portion of the restiform body had apparently escaped, but above the lesion the degeneration appears complete. The uppermost and outer portions of the nuclei cuneati are undoubtedly slightly involved in the cicatrix and there is perhaps slight pallor of the internal arcuate fibres from the nuclei cuneati. At higher levels the lemnisci, however, appear normal. Most of the olivary fibres are involved, but those which enter the restiform body above the lesion escape. The external cuneate nucleus on each side is more damaged. The degenerated restiform bodies can be clearly seen (fig. 8), and the intact fibres of the I.A.K. bundle or vestibulo-cerebellar connections stand out in contrast. Fig. 9 shows the degenerated fibres radiating out to the vermis. The lesions undoubtedly involved the restiform bodies at about their middle. The fibres interrupted by the lesions are those of the spino-cerebellar tracts, those from the nuclei lateralis medulla, those from the external cuneate nucleus and probably the caudal olivo-cerebellar fibres of both sides.

IV.—Discussion.

Section of the dorsal spino-cerebellar tract in our animals produced definite and constant symptoms. These were not complicated by associated damage of the pyramidal tract, for sections of the spinal cords showed no degeneration in this tract. The symptoms were slight ipsilateral weakness, some degree of hypotonia, diminution of the reflexes, slight dysmetria, and in the acute stage a diminution in the hopping and placing reflexes. In the acute stage the animals occasionally fell towards the side of the lesion and the ipsilateral limbs were abducted. These disturbances were transient and had practically disappeared by the end of two or three weeks. Later it was difficult to distinguish one of these animals from a normal monkey.

The same symptoms, but in varying degrees, were found when the lesions involved the restiform body at different levels, provided there were no vestibular complications. Even when the lesion was near the entrance of the eighth nerve we failed to find the rolling movements described by previous authors, as by Biedl in the cat and by Ferrier and Turner in the monkey. These occurred only when the lesion extended deep enough to involve the vestibular apparatus. On the other hand, rolling movements were observed in animals in which we systematically produced lesions of the vestibular system. These will be reported in detail in a subsequent publication.

It is of interest that the symptoms, although similar in type to those produced by section of the dorsal spino-cerebellar tract in the cord, were

greater in intensity when the lesions involved the restiform body in the medulla. The severity of the disturbances seems to increase the higher the level at which the lesions injured the restiform body, indicating the involvement of fibres of other sources with similar types of function, for example, the large bundle of fibres from the external cuneate nucleus which enters the outer side of the ipsilateral restiform body. The external cuneate nucleus, which has been variously described as the nucleus of Monakow, the nucleus of Blumenau, the nucleus corporis restiformis, nucleus cuneatus externus, &c., receives fibres by way of the funiculus cuneatus from the cervical and upper dorsal roots, and sends fibres into the ipsilateral restiform body. This nucleus of Clarke-Monakow, as we prefer to call it in honour of Clarke [58] who first decribed it, and Monakow [42], who first recognized its cerebellar connections, undergoes atrophy when the cerebellum is removed or when the inferior peduncle is cut at a high level, indicating that the nucleus sends its fibres into the inferior cerebellar peduncle. In one animal in which we injected alcohol into the caudal half of this nucleus, the symptoms were similar to those of the lesion of the dorsal spino-cerebellar tract. Many authors as Gudden, Monakow, Edinger, Flechsig, Mingazzini, Lewandowsky, Mussen, &c., have stated that each dorsal column nucleus sends fibres into the restiform body, particularly into that of the opposite side, which originate, according to them, from the nuclei gracilis and cuneatus, irrespective of the nucleus of Clarke-Monakow (anterior external arcuate fibres). The posterior external arcuate fibres from the nuclei gracilis and cuneatus reach the homolateral restiform body. And according to Klimoff, Darkschevitch and Freud, Goldstein, &c., crossed and direct fibres from the posterior columns pass directly into the cerebellum. The existence of these fibres is still a matter of doubt.

In addition to these contingents of fibres our work has shown that the nucleus of Clarke-Monakow (external cuneate nucleus) establishes an important connection between the dorsal roots from the upper extremities and neck and the inferior cerebellar peduncle. Section of the restiform body above the level of this nucleus may therefore be expected to produce more intense symptoms than lesions of the dorsal spino-cerebellar tract in the spinal cord.

Another addition to the upper part of the restiform body is the large olivo-cerebellar contingent, arising from the opposite olive. These fibres enter the restiform body on its mesial aspect at the level of entrance of the eighth nerve.

A further group of fibres is received from the so-called nucleus lateralis medullæ. This nucleus undergoes atrophy after lesions of the ipsilateral inferior cerebellar peduncle even at fairly low levels.

It may therefore be expected, in view of the numerous contingents which enter the restiform body as it passes upwards, that the symptoms associated with lesions of it at various levels may vary. The intensity of the disturbances increases as the lesions lie more cephalad, but no new symptoms appear. The tendency to fall to the side of the lesion particularly, increases as the lesion lies higher in the restiform body.

It may be noted that in our descriptions of the animals, most of the symptoms appeared to be explicable on the basis of deficient afferent impulses to the cerebellum from the limbs. There were no symptoms of abnormal activity such as rolling movements, spontaneous tremor at rest (except transitory tremor in the acute stage) intention tremors, or spontaneous nystagmus in pure lesions of the spino-cerebellar tract or restiform body. Such symptoms have been described by almost all previous authors who have experimented on the inferior cerebellar peduncle in the monkey and other animals. There is little doubt that these active symptoms are due to complicating factors such as extension of the lesion beyond the restiform body proper. They occurred in many of our other animals in which the lesions extended into the vestibular nuclei or involved the secondary vestibular connections such as the I.A.K. bundle (juxtarestiform body). In these animals the symptoms differed from those in which the restiform body or dorsal spino-cerebellar tract only were injured, and included rolling movements toward the side of the lesion, spontaneous tremors, abnormal postures of the head, spontaneous nystagmus, &c. As the vestibular nuclei and the secondary vestibular connections lie close to the restiform body, especially in its higher levels, in the absence of serial anatomical controls small but significant lesions which may complicate the symptoms can be missed easily.

An interesting feature of the experiments is the ability of the animals to compensate practically completely the disturbances of cerebellar function due to bilateral lesions of the restiform body. After two or three weeks, even in the presence of bilateral lesions which interrupt all the afferent impulses from the limbs to the cerebellum by way of the restiform body, the animal may jump about, climb and use its limbs practically as well as a normal monkey. The other sources of afferent impulses to the cerebellum are the middle peduncle from higher levels and the vestibular connections between the medullary

vestibular nuclei and the nuclei of the cerebellar roof, but none of these are directly related to the limbs. It is of interest that the symptoms are more persistent if, in addition to injury of the restiform bodies, there are lesions of the vestibular apparatus, either of the vestibular nuclei or of the I.A.K. bundle. Then the animal may never, at least within eight or nine months, compensate to any great extent the combined disturbances.

Another point of interest is the comparison between the results of lesions of the dorsal spino-cerebellar tract in the high cervical region with those following unilateral section of the dorsal columns at the same level. The disability due to the latter is much more marked and differs in type too. In the first place lesions of the dorsal columns lead to practically complete loss of spontaneous movements in the limbs; the animal does not grip any object spontaneously and seems incapable of closing its fingers around any object of support, while the animal with a lesion of the dorsal spino-cerebellar tract is perfectly capable of reaching out with the arm or leg of the affected side and of grasping a support accurately and with good strength. Lesions of both the dorsal columns and of the spino-cerebellar tract are associated with diminution in muscle tone as determined by resistance to passive movements, but this is more marked in the presence of lesions of the dorsal column. When the dorsal columns are injured the deep reflexes are active and even appear at times to be over-active, while in lesions of the dorsal spino-cerebellar tract they usually appear slightly decreased. That this is not due to involvement of the pyramidal tract is shown by the fact that similar decrease of the knee-jerks is found when the lesion is made in the restiform body above the level at which the pyramidal fibres could possibly be injured.

Animals with lesions of the restiform body, regardless of the level, are always perfectly capable of grasping objects spontaneously and of using the limbs in practically every type of movement. When the dorsal-column nuclei are injured they lose the ability to perform spontaneous movements with the limbs and are incapable of grasping objects or particles of food, exactly as when the dorsal columns are divided.

In a previous communication on the effects of lesions of the dorsal columns [59] we have shown that when they are injured by lesions in the cervical segments the symptoms are more severe in the fore-limbs than in the hind-limbs. This was attributed to the combination of dorsal column elements and cerebellar elements in the dorsal columns at these

levels. The cerebellar elements are those which enter the dorsal columns to pass to the ipsilateral restiform body by way of the external cuneate nucleus (nucleus of Clarke-Monakow). The direct pathway for cerebellar representation from the upper limb has, in contrast to that from the hind-limb, been always obscure. It has been assumed that the dorsal spino-cerebellar tract carries impulses only from the trunk and hind limbs, but in our experimental animals in which only the dorsal spino-cerebellar tract was injured in the cervical region, the ipsilateral fore-leg was affected in the same manner as it was by lesions of the restiform body, and the symptoms in it were just as severe as those in the hind-limb. This indicates that in addition to the dorsal column cerebellar component from the upper limbs there must be another component which reaches the inferior peduncle by way of the dorsal spino-cerebellar tract.

Our present work has not established accurately the origin and terminations, or even the minute anatomy, of the dorsal spino-cerebellar tract, but it shows that after reaching the restiform body the fibres of this tract tend to take a lateral course in the restiform body while the fibres from the various medullary components are added to the mesial portion of the restiform body. At higher levels this position is possibly reversed, inasmuch as the fibres from the olive, for example, may reach the lateral lobes of the cerebellum whereas those of the dorsal spino-cerebellar tract ultimately pass to the vermis. This would necessitate a crossing of these fibres somewhere in the course of the inferior cerebellar peduncle.

V.—Conclusions.

(1) Section of the dorsal spino-cerebellar tract in *Macacus rhesus* monkeys, unassociated with any pyramidal tract involvement, produces a definite group of symptoms consisting of ipsilateral weakness of the limbs, slight hypotonia, diminution of the reflexes, slight dysmetria and, in the acute stage, a diminution in the hopping and placing reflexes; occasionally, in the acute stage, the animal tends to fall toward the side of the lesion, and the ipsilateral limbs while at rest assume abducted postures.

(2) The disturbances practically disappear by the end of two or three weeks. Later it is difficult to distinguish one of these animals from a normal monkey. Only a slight loss of elasticity in the ipsilateral limbs may persist.

(3) The symptoms associated with section of the restiform body are

the same in type as those which result from section of the dorsal spino-cerebellar tract. The only difference is one of intensity, as the lesions of the restiform body are followed by a more pronounced dysmetria, hypotonia, ipsilateral weakness and diminution of the reflexes.

(4) The symptoms are the same in type regardless of the level at which the restiform body is divided, but their intensity is greater, the higher the lesion is placed. The explanation is that lesions in the upper part of the restiform body involve new contingents of fibres from various structures which join the restiform body to enter the cerebellum (contingent from the nucleus funiculi lateralis, contingent from the nucleus of Clarke-Monakow and contingent from the olives).

(5) We have never observed after section of the restiform body forced postures or movements, such as rotation around the long axis of the animal, or deviation of the head or chin to one or the other side. These phenomena do not, therefore, constitute an integral part of the symptomatology of lesions of the restiform body as previous investigators have stated. They appear only when the vestibular apparatus (vestibular nuclei or I.A.K. bundle) is also injured.

(6) The lesions of the dorsal spino-cerebellar tract in the higher cervical segments of the cord is followed by disturbances in the ipsilateral upper extremity. We therefore assume that part of the cerebellar representation of the upper limbs must be established through the dorsal spino-cerebellar tract. There is also another pathway which connects the posterior columns with the cerebellum by way of the external cuneate nucleus or nucleus of Clarke-Monakow.

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THE MECHANISM OF INTERNAL HYDROCEPHALUS IN SPINA BIFIDA.

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THE frequent association of hydrocephalus with spina bifida has been observed for centuries but no explanation of this association has yet proved generally acceptable. Morgagni (1769) thought that the hydrocephalus was the primary disorder and that the excess of fluid present caused the spinal defect and the bulging sac at the site of this bony deficiency. Both he and subsequent observers had difficulty, however, in accounting for the occurrence of spina bifida without hydrocephalus. In the latter part of the last century the association came to be explained in terms of teratogenesis but without any precise conception of the mechanical factors responsible for the hydrocephalus. At that time little was known, however, of the way in which the cerebrospinal fluid is formed and circulates. The work of Lewis Weed (1914) and of Dandy and Blackfan (1914) has thrown much light on these problems and has led to the recognition of "communicating" and "non-communicating" types of internal hydrocephalus. In the former a dye injected into one or both lateral ventricles can be recaptured within a few minutes from the lumbar subarachnoid space; in the latter this is rendered impossible by the presence of a block which prevents in some part of its course the passage of cerebrospinal fluid from the lateral ventricles to the spinal subarachnoid space.

In this paper a mechanical explanation is offered of the production of communicating hydrocephalus in a series of cases of meningomyelocele. Further, the examination of a single case of meningocele without hydrocephalus suggests that the same mechanism may sometimes operate also in this type of spina bifida. To determine the factors responsible for hydrocephalus in any given instance it is desirable that

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the anatomical study should be carried out in the light of a clinical test to discover whether the hydrocephalus is of the communicating or of the non-communicating type. Unfortunately this has been practicable in only a few instances. The study of pathological anatomy alone may, however, give a satisfactory clue to the nature of the hydrocephalus.

Meningo-myelocele.

(1) *Material.*

A series of ten consecutive cases of lumbo-sacral or dorsi-lumbo-sacral meningo-myelocele have been examined. Their principal clinical and anatomical features are presented in the accompanying

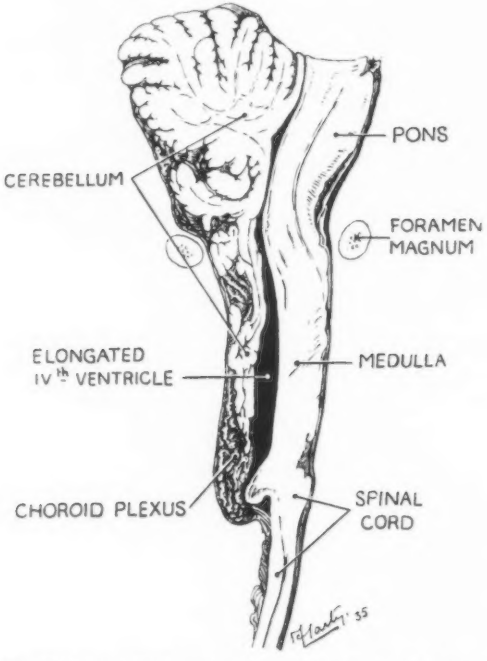

Fig. 1.—Case 10. Median sagittal section through brain-stem to show Arnold-Chiari malformation. Gross elongation of medulla.

table. Internal hydrocephalus was present at birth in all except two examples (Cases 4, 6). In two only of the eight cases in which hydrocephalus was present was it demonstrated, by the injection of dye or india ink, to be of the non-communicating type

(Cases 5, 8). In Case 5 there was atresia of the Sylvian aqueduct and in Case 8 the foramina of Luschka and Majendie were imperforate. A communicating hydrocephalus was present in three examples (Cases 2, 3, 7). In Case 7 this was demonstrated by the injection of india ink into the ventricles. In Case 2 there was an ascending purulent meningitis and it was evident, from the path of the infection, that the hydrocephalus was of the communicating type.

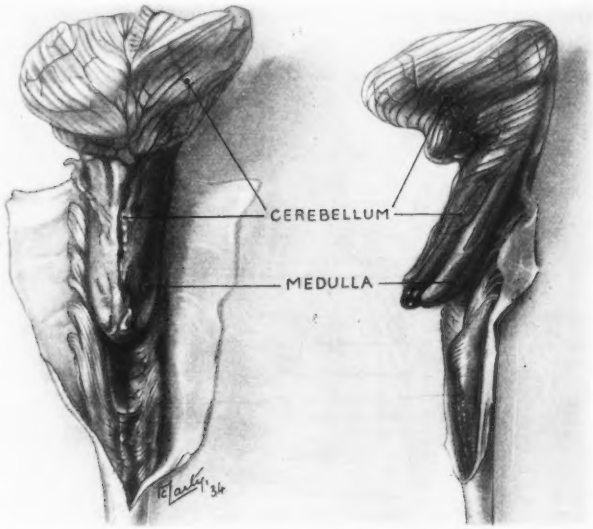

FIG. 2.—Case 8. Dorsal and lateral view of Arnold-Chiari malformation.

In Case 3 a similar conclusion was reached from the anatomical examination. In the three remaining cases (1, 9, 10) the determination of the type of hydrocephalus present was not practicable.

In both of the cases (4, 6) in which hydrocephalus was absent the cerebrospinal fluid escaped freely from the body through a fistula in the membrane covering the spinal defect; hence there was no back pressure along the cerebrospinal pathway and no hydrocephalus. In Case 4 the infant survived birth for eleven days and pyocephalus developed as a result of an ascending infection of the cerebrospinal pathway.

(2) *Malformation.*

In all ten examples a remarkable malformation of the hind-brain was observed. In this a tongue of variable length, consisting of cerebellar

tissue and the greatly elongated medulla oblongata, protrudes downwards into the spinal canal (figs. 1, 2). It overlaps and compresses the upper segments of the cervical cord, distending the dural theca in this neighbourhood and filling the foramen magnum. The cavity of the fourth ventricle extends caudally into this tongue, lying between the cerebellar and medullary components. The maximum diameter of the ventricle is usually within the vertebral canal at and below the level of the foramen magnum, and here too or at a still lower level are found the choroid plexuses and the foramina with which they are associated. The plexuses are sometimes united into one mass which lies in the middle line in the ventricular cavity (fig. 4). The

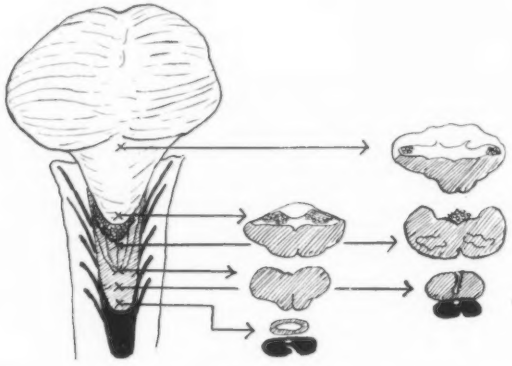

FIG. 3.—Diagram of the malformation in Case 4. Unshaded part = cerebellum; diagonally shaded part = medulla oblongata; black = spinal cord; granular areas = choroid plexus.

floor of the ventricle, formed by the elongated medulla oblongata, presents the characteristic markings of the rhomboid fossa, and in the middle line towards its caudal extremity is a minute pore which provides a horizontal communication between the ventricle and the central canal of the ventrally placed spinal cord. The cavity of the ventricle usually extends beyond this pore as a diverticulum into the tip of the tongue-like mass. Cross-sections of the brain-stem show a somewhat complicated pattern according to the number of structures involved. Examples are diagrammatically shown in figs. 3 and 4; these also demonstrate the variations that exist in the relative lengths of the cerebellar and medullary components found in the malformation. These diagrams and the drawing in fig. 2 represent dissected specimens; in the undissected

specimen the malformation is greatly obscured by the investing leptomeninges which are usually thick, gelatinous and remarkably vascular.

A number of other structural abnormalities are commonly found in association with this malformation. The spinal cord appears abnormally small and the cervical roots always run in a cephalic direction to reach their exits through the dura mater (fig. 2). Their cephalic direction decreases as successive segments are examined until, in the upper thoracic region, they are either horizontally or caudally inclined.

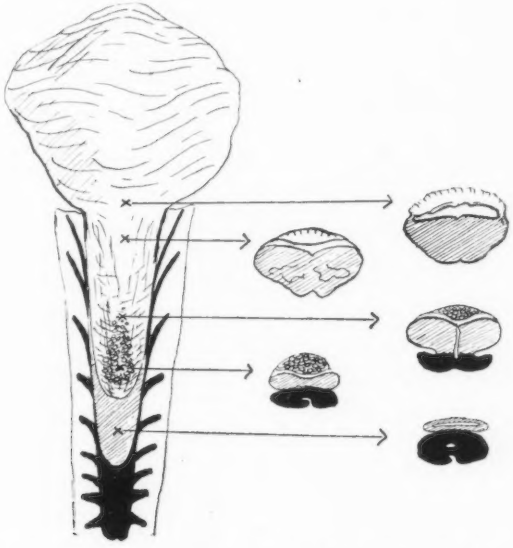

FIG. 4.—Diagram of the malformation in Case 9. Conventions as in fig. 3.

Hydromyelia is commonly present in a variable number of consecutive segments in the cervical and thoracic cord. There is a conspicuous hypoplasia of the cerebellum which is usually composed of a small compact mass lacking differentiation into vermis and lateral lobes. The tonsils and flocculi can seldom be identified. The pons as well as the medulla oblongata is elongated and lacks the characteristic ventral protuberance. It is poorly demarcated from the medulla. In addition the cranial nerve roots arising from the pons and medulla are greatly elongated; for example, in Case 6 the sixth roots measured 2·1 cm. to their foramina, the eighth roots 1·7 cm. and the fifth roots 1·3 cm. The

corpora quadrigemina are poorly defined and are sometimes fused into a single conical mass.

This curious maldevelopment was noticed first by Arnold (1894) in a case of spina bifida described as an example of "Myelocyste"; it was more fully described in the following year by Chiari in a series of seven cases of spina bifida, one only of which was more fully particularised as an example of meningo-myelocele. A good description in five cases of meningo-myelocele was published by Solovtzoff (1901), but perhaps the best and fullest account is that of Gredig and Schwalbe in four cases of meningo-myelocele (1907). The last-mentioned authors give a detailed study of the dislocation of nerve-tracts caused by the malformation and it is not proposed, therefore, to describe the microscopic anatomy in the present series. They called this lesion the *Arnold-Chiari malformation* and it is convenient to adopt this name.

(3) *Relation of the Malformation to Hydrocephalus.*

The elongated fourth ventricle extends for a considerable distance below the foramen magnum. It follows that if the foramina of Luschka and Majendie are patent the cerebrospinal fluid escapes into the subarachnoid space within the vertebral canal. The plugging of the upper cervical part of the canal by the Arnold-Chiari malformation is likely to hinder any upward flow of fluid into the subarachnoid channels within the posterior fossa, into which it normally passes on its way to escape through the cranial arachnoid villi. According to the experiments of Dandy and Blackfan (1914) the greater proportion (three-fourths to four-fifths) of cerebrospinal fluid is absorbed from the surface of the brain and from one-fourth to one-fifth only from the spinal canal. Accepting this estimate it follows that occlusion of the foramen magnum in these cases of spina bifida will lead to a damming back of cerebrospinal fluid in the ventricular system and hence to internal hydrocephalus. Certain evidence can be advanced in support of this hypothesis from study of our series of cases.

Experimental evidence.—In Cases 4 and 7 a suspension of india ink was introduced into the lateral ventricles when death was imminent and the distribution of the particles examined at necropsy. On naked eye examination there was a profuse deposit of pigment throughout the ventricular system and in the subarachnoid space of the spinal canal below the level of the Arnold-Chiari malformation. Above this level the leptomeninges in Case 4 appeared to be devoid of pigment, although on microscopic examination a few particles were found within macro-

phages in the leptomeninges over the mid-brain. In Case 7 a moderate amount was visible at the base of the brain and a very little in the sulci over the cerebral convexities. From this it is inferred that an appreciable though incomplete blockage was present at the foramen magnum in both cases, the degree being greater in Case 4 than in Case 7. Patency of the leptomeningeal spaces over the cerebral convexities was

CASES OF MENINGO-MYELOCELE.

No.	P.M. No.	Sex and Age	Site of spina bifida	Hydrocephalus	Arnold-Chiari malformation	Remarks
1	219.30	M. 8/365	Lumbo-sacral	Congenital; type undetermined	Present	C.N.S. received for investigation after necropsy
2	334.31	F. 4/52	Dorsi-lumbo-sacral	Congenital (communicating)	Present	Ascending meningitis. Type of hydrocephalus inferred from path of infection
3	386.32	M. 2/365	Dorsi-lumbo-sacral	Congenital (communicating)	Present	Type of hydrocephalus inferred from anatomical examination of brain stem
4	463.32	M. 11/365	Lumbo-sacral	Acquired pyocephalus (communicating)	Present	Fistula at spinal defect. Ascending infection followed by pyocephalus. India ink injected into lateral ventricles just before death
5	235.33	F. Still born	Lumbo-sacral	Congenital (non-communicating)	Present	Methylene blue injected into lateral ventricles before necropsy. Atresia of Sylvian aqueduct
6	339.33	F. 2/365	Lumbo-sacral	Absent	Present	Fistula at spinal defect. Methylene blue injected into lateral ventricles before necropsy escaped freely through fistula.
7	395.33	F. 7/365	Lumbo-sacral	Congenital (communicating)	Present	India ink injected into lateral ventricles just before death
8	396.33	F. 7/365	Dorsi-lumbo-sacral	Congenital (non-communicating)	Present	India ink injected into lateral ventricles before death. Imperforate 4th ventricle foramina
9	164.34	M. Still born	Lumbo-sacral	Congenital; type undetermined	Present	Post-mortem softening too advanced to investigate type of hydrocephalus
10	501.34	F. Still born	Dorsi-lumbo-sacral	Congenital; type undetermined	Present	Perforation of brain to facilitate delivery

also demonstrated by the distribution of the particles in Case 7, so that a defect in this respect cannot be advanced as an alternative explanation of the hydrocephalus in this case.

Pathological evidence.—In two instances (Cases 2 and 4) there was an ascending purulent leptomeningitis and pyocephalus following infection of the tissues at the site of the spinal defect. Examination of these specimens, both macroscopically and microscopically, showed a severe purulent infiltration of the spinal meninges up to the level of the Arnold-Chiari malformation, but above this level the inflammatory reaction was mainly confined to the ventricular system where a conspicuous pyocephalus was present. In neither instance was there any macroscopic infiltration of the basal meninges, but microscopically a slight degree of infiltration was found about the mid-brain in both. These findings suggest some degree of obstruction at the foramen magnum to the upward passage of organisms within the leptomeningeal spaces.

Other evidence.—Lastly, certain clinical observations are relevant to this discussion. It has for long been known that operative removal of the sac in spina bifida is frequently followed by hydrocephalus when this was not present before the operation. Now it has been shown by Penfield and Cone (1932) that the soft tissues of the sac absorb cerebrospinal fluid, and these authors claim that hydrocephalus can be avoided if the walls of the sac are conserved. They explain this result by postulating that the normal mechanism for the absorption of the fluid is imperfectly developed in these subjects (private communication). But in terms of the theory advanced in this paper the development of hydrocephalus after operative removal of the sac can be simply explained as a decompensatory effect. It is not unreasonable to suppose that the extra absorbing apparatus provided by the sac may be just sufficient to balance the degree of obstruction at the foramen magnum in instances where such obstruction is not severe. If this is true then operative removal of the sac will disturb this balance and will be followed by the development of internal hydrocephalus.

Meningocele.

The material so far described has been limited to meningo-myelocele. Hydrocephalus has also been observed in many cases of meningocele; in some of these it has been congenital and in others it has followed operation. Inasmuch as these are more favourable cases for surgical treatment than examples of meningo-myelocele, it is of practical

importance to discover whether they also are liable to present any malformations of the brain stem. From this point of view it is unfortunate that no comparable series of cases has been available for anatomical study. One example only of meningocele has come to necropsy within the period of this study. This will be fully described because it possesses features that, in our view, bring this class of case into line with those already described.

Clinical. Reg. No. 21882. 1934. Surgical. A female infant was admitted when three days old to the London Hospital on July 16, 1934, under the care of one of us (C.D.) with a translucent cystic meningocele, about 6 cm. diameter, over the sacrum. There was no hydrocephalus and no further demonstrable abnormality in the nervous system. Operative interference could not be delayed on account of threatened rupture of the sac. On August 7 the greater part of the sac was removed because it was too tenuous and poorly nourished to be preserved. What remained of the underlying meninges was puckered up, and the muscles on either side were freed and approximated in the middle line. The skin when sutured was under tension. On August 11 the wound was slightly inflamed, and two days later the temperature began to rise, reaching 103° F. on the 15th and 105° F. on the 20th. On August 23 the temperature returned to normal and after that fluctuated. Lumbar puncture on August 30 produced blood and pus from which a pure culture of a coliform bacillus was grown. One month after the operation there was definite expansion of the skull and the infant was weaker. Head retraction was present and varied from day to day. Further lumbar punctures on September 8 and 26 produced "pure pus" and "turbid fluid" respectively. The infant died on October 25, 1934, aged 15 weeks.

Summary of Necropsy (*P.M.* 423. 1934). *Bronchopneumonia. Pyocephalus. Ascending purulent* (Bacillus coli) *cerebrospinal meningitis. Operation: Plastic repair of lumbo-sacral meningocele. Spina bifida.*—Slight œdema of myocardium. Œdema and congestion of liver, spleen and kidneys. Very little glandular tissue in thymus. Moderate amount of lipoid in suprarenal bodies. Severe mucous catarrh of stomach. Greyish green pus in both middle ears. An extremely wasted female infant.

Examination of brain.—The skull was slightly expanded, measuring 38 cm. in circumference, 22 cm. from nasion to inion and 28 cm. coronally between the external meati. The bones of the vault were widely separated. On opening the skull the convolutions were flattened and dry. During manipulation of the brain a considerable quantity (over 250 c.c.) of thin green pus escaped from the lateral ventricles. There were light adhesions between the arachnoid and dura at the base of the brain. Golden streaks of inspissated pus were present in the leptomeninges in the proximal parts of the Sylvian fissures and the adjacent surfaces of both temporal poles. Similar deposits were present over the dorsal and posterior aspects of the cerebellum and to a less extent on the ventral surface of the pons. The lateral ventricles were greatly dilated

and the ependymal surfaces were coated with a thick layer of green pus. The cavity of the third ventricle and the Sylvian aqueduct were filled with inspissated golden pus. (The subtentorial part of the brain and the spinal cord were removed together with the dural theca and were fixed in formalin before further examination).

Apart from a diffuse chronic purulent spinal meningitis the principal features are illustrated in fig. 5. The cerebellum is well formed and appears to be of full size. The medulla oblongata occupies the uppermost part of the vertebral canal and is seen from the dorsal aspect as a smooth area (1 cm. long by 1·35 cm. from side to side) which is embraced on either side by the

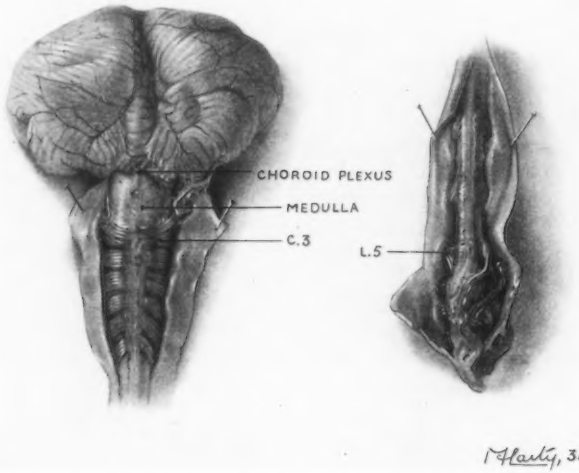

FIG. 5.—Dorsal views of hind-brain and lumbo-sacral cord in case of meningocele (P.M. 423, 1934).

upwardly directed roots of the upper two cervical segments. This appearance of the medulla recalls the Arnold-Chiari malformation seen in the series of cases of meningo-myelocele, but on dissection there is no overlapping of the spinal cord by a tongue of folded medulla oblongata such as is seen in the fully developed malformation. Further dissection shows, however, a dislocation of the choroid plexuses of the fourth ventricle: a large tuft (0·6 cm. by 0·4 cm.) occupies the middle line between the tonsils in the position of the foramen of Majendie. From this the right choroid plexus loops downwards and forwards in the leptomeninges following the lower border of the tonsil and appears to terminate in the right foramen of Luschka. The left plexus is not visible from the exterior but lies within the ventricle, uniting the central intertonsillar mass with the left lateral recess. The cavity of the fourth

ventricle is collapsed and is filled with inspissated pus. It is continued downwards just beneath the mid-dorsal line throughout the elongated portion of the medulla oblongata and passes thence to the central canal of the spinal cord, becoming more ventrally placed in the transition. The pons is well formed and is clearly demarcated from the medulla. The sulcus separating them is unusually low in relation to the cerebellum, being only 0·6 cm. above the tips of the tonsils. On transverse section the medulla appears well formed; the olives are present at the same level as the inter-tonsillar mass of choroid plexus and are traceable downwards to a point 0·2 cm. above the junction of medulla and spinal cord.

Spine and spinal cord.—A completely healed cruciate operation scar (7 cm. from above down by 5·5 cm. from side to side) extends from the second lumbar vertebra to within 1·7 cm. of the tip of the coccyx and laterally over the iliac crests. Beneath this is an oval deficiency (3·7 cm. long by 1·5 cm. at widest) due to the non-union of the laminæ of the lowest three lumbar and all the sacral vertebræ. This gap is filled in with scar tissue uniting the skin with the subjacent meninges. The appearances on dissecting the lowest part of the spinal cord are represented in fig. 5. The cord, which extended into the lowest part of the sacrum, ends in a bulbous expansion measuring 1·7 cm. from above down by 1·1 cm. from side to side by 0·6 cm. thick. There is no lumbar enlargement and no cauda equina. The lumbar cord is 4·5 cm. long and is similar in calibre to the thoracic cord. Its roots are given off almost horizontally and the lower filaments of the fifth segment are even cephalic in direction. The anatomy of the sacral roots was not satisfactorily elucidated, partly because the bulbous expansion was enveloped in scar tissue and partly, as transverse sections revealed, because an upward folding of the most caudal part of the cord led to an appearance of duplication just above the middle of the expansion and to a complete distortion of the pattern below this level. As shown in the figure, however, three roots pass in segmental fashion through the dura on the left side while two other roots cross the posterior surface of the expansion upwards and to the right to pass through the dura with the fifth right lumbar root and opposite the first left sacral root respectively. Throughout the thoracic and lumbar regions the centre of the cord is occupied by a lenticular or polygonal area (up to 0·3 by 0·1 cm. in the 4th lumbar segment) of yellowish appearance with, in places, a rusty-brown border.

Microscopic examination.—The leptomeninges throughout the spinal cord and the brain-stem show considerable fibrous thickening and are infiltrated with many plasma cells, small lymphocytes and a few neutrophil leucocytes. The central canal of the spinal cord and the cavity of the fourth ventricle are filled with similarly infiltrated, sclerotic tissue corresponding with the yellowish areas observed in the spinal cord with the naked eye. The yellowness is due to the presence of considerable collections of foam cells. These changes in the meninges, fourth ventricle and central canal are doubtless a result of the infection. The anatomical appearances described in the hind-brain and spinal cord are confirmed. The medulla is well-formed. Sections taken through

the bulbous enlargement of the sacral cord at the levels of the left, second and third roots show, on either side, a deep lateral cleft. The outline of the cord thus resembles a flattened cottage loaf. In the more caudal of the two sections the spinal cord is almost completely divided into dorsal and ventral parts. The pia occupying the left lateral cleft in the higher of the two sections contains three epidermoid cysts, the largest of which (2 by 0·9 mm.) lies at the ventral lip of the cleft and the other two at the dorsal lip and the depth of the cleft respectively. The cysts are lined with squamous and prickle-celled epithelium and are filled with thin concentric laminæ of exfoliated material. They are evidently a developmental abnormality.

Discussion.

We have described ten consecutive examples of the Arnold-Chiari malformation in cases of meningo-myelocele, and have shown how the deformity may be the cause of the hydrocephalus. In the literature upon the Arnold-Chiari malformation the exact nature of the spinal defect is not always stated. Thus in Arnold's one case the defect was described as a "Myelocyste," while in six of Chiari's seven cases it was simply labelled as spina bifida. Where, however, the nature of the defect is clearly stated it has been a meningo-myelocele.

Hydrocephalus is, however, also sometimes associated with meningocele, as is shown by clinical records. Such anatomical studies of this condition as we have discovered in the literature, and they have been very few, have not thrown any light upon the possible occurrence of malformations of the hind brain in this class of case. Nor have they given an explanation of the hydrocephalus which is sometimes found. Detailed descriptions of the central nervous system in spina bifida occulta have been published more frequently and there is no doubt that in this condition the hind-brain is usually normal. We have dissected the brain and cord in two examples of spina bifida occulta and in neither have we found any abnormality in the brain-stem. Hydrocephalus was absent.

Our single case of meningocele shows, however, that the incidence of malformations of the medulla oblongata and fourth ventricle of the Arnold-Chiari type is not limited to examples of meningo-myelocele. In the present instance it is clear that the deformities were of a far less severe order than those described as characteristic of the Arnold-Chiari malformation, although they appear to be of a similar kind. There was no hydrocephalus. The demonstration, however, of a minor degree of the malformation in a case of meningocele without hydrocephalus suggests the possibility that greater degrees of the malforma-

tion may be the cause of the hydrocephalus that complicates some examples of meningocele.

Our theory awaits confirmation. If hydrocephalus, either congenital or post-operative, were due to such a malformation, then air injected by the lumbar route would collect in the ventricles and not in the sulci upon the cerebral convexities. Such a result would be not only of academic interest but of clinical importance. It would point to the desirability of decompressing the spinal cord at the foramen magnum to facilitate the circulation of fluid in the leptomeningeal spaces. Such an operation has not yet been carried out.[1]

SUMMARY.

Attention is drawn to the Arnold-Chiari malformation as a possible cause of internal hydrocephalus in spina bifida.

The malformation was found in ten consecutive examples of lumbo-sacral or dorsi-lumbo-sacral meningo-myelocele.

A comparable but far less pronounced malformation of the medulla oblongata is described in a case of lumbo-sacral meningocele without hydrocephalus. It is suggested that a more typical Arnold-Chiari malformation may be the cause of the hydrocephalus that complicates some examples of meningocele.

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[1] Our attention has been drawn, while this paper was in the press, to a monograph entitled "Over Hydrocephalus," presented as a thesis for the doctorate in medicine in the University of Leiden by C. J. van Houweninge Graftdijk in 1932. The author discusses in this the probability that the Arnold-Chiari malformation acts as a valve, but he believes that it acts in a manner contrary to that suggested in our paper. He brings forward evidence that the cerebrospinal fluid can escape readily in an upward direction from the vertebral canal into the ventricles or cerebral meningeal spaces but has difficulty in passing from the ventricles down into the vertebral canal. He has endeavoured to relieve this obstruction either by resecting the tongue of redundant tissue or by resection of the bone over the posterior surface of the malformation and incision of the underlying dura. His cases, however, have died either from the effects of the operation or from post-operative complications.

PAIN: THE PERIPHERAL PATHWAY.

BY G. K. STÜRUP (COPENHAGEN)[1] AND E. ARNOLD CARMICHAEL.

In order to explain the appreciation of pain in a limb apparently rendered analgesic by a lesion of the plexus or by section of the spino-thalamic tracts, it has been suggested that pain impulses may utilize the periarterial plexus or sympathetic chain to gain entrance to the spinal cord.

In this paper are described experiments which were carried out to test these postulates.

EXPERIMENTS.

Two healthy young male adults were submitted to the following procedure:—

Subject A.—The left ulnar nerve was blocked by a perineural injection of a solution of 4 per cent. novocain, containing 1:100,000 adrenalin, where the nerve lies in the groove of the medial epicondyle of the humerus. When complete sensory loss in the distribution of the ulnar nerve was obtained, as judged by a failure to appreciate superficial and pressure pain as well as passive movement of the interphalangeal joints of the fifth digit, the digital artery and nerve at the ulnar side of the base of the fifth digit were exposed by open dissection. The artery with its adventitia was then laid, in a dry field, across two platinum electrodes connected to a secondary coil of a faradic battery. Stimulation was then applied to the artery with the secondary coil in various positions. During repeated stimulation of various durations and strengths no sensation of any character was perceived by the subject. The strength of the current used was more than sufficiently strong to give rise to pain when the electrodes were applied to the tip of the tongue and to contract the underlying muscle when applied to the skin. Stimulation of the exposed nerve in a like manner resulted in no pain or other sensation. The artery was then pulled, stretched and clamped

[1] This work was carried out on behalf of the Medical Research Council at the Research Unit, National Hospital, Queen Square, London, while Dr. Stürup held a Rockefeller Foundation Fellowship. One of the observations was reported in the Oliver-Sharpey Lectures, 1933, at the Royal College of Physicians by one of us (E.A.C.).

with forceps again without resultant sensation. During the procedure pain and other sensations were appreciated from the radial border of the hand on appropriate stimulation.

Doctors Robertson and Nevin kindly carried out the surgical procedure and to them we are grateful for their help.

Subject B.—A similar procedure was carried out with the following differences. The novocain solution was a 2 per cent. solution: after exposure of the artery and nerve, the artery alone was stimulated with a current from a secondary coil of a faradic battery. No conscious sensation was apparent during the stimulation, though at one time the electrical stimulus was much greater than necessary to produce contraction of muscle through intact skin.

Mr. Julian Taylor kindly carried out the surgical procedure and to him we are grateful.

Conclusion from Experiments.

The perineural anæsthetization of the ulnar nerve as it lay in the groove of the medial epicondyle of the humerus produced a complete anæsthesia of the tissues supplied by the ulnar nerve distal to the site of the injection. It may be confidently asserted that the local injection of novocain did in no way reach the periarterial plexus surrounding the brachial artery as the latter lay anterior to the elbow-joint. The digital artery exposed at the dissection is a branch of the ulnar artery, itself a branch of the brachial artery.

Accordingly were there pain conducting fibres or fibres competent to carry impulses appreciated as pain travelling centripetally along the digital artery and its arteries of derivation, the novocain injection could not have reached them. As no pain or sensation resulted from stimulation of the openly dissected artery, it is only possible to assume that no centripetal sensory pathway from the digital artery was available along the digital, ulnar and brachial arteries, when the ulnar nerve was blocked at the elbow.

It is not to be assumed from these experiments that sensory fibres and endings are not to be found on arteries, for the evidence in favour of this is overwhelming. Pain resulting from experimental puncture of an artery is a well-established fact, also pain from the placing of hæmostatic forceps on an artery. The experiments described only afford proof that such sensory fibres travel but a short distance along the artery before they leave it to join a peripheral nerve.

Discussion.

The literature dealing with the relief of pain by sympathectomy or by stripping an artery of its adventitia is of large proportions. The observations made by many have led to a controversy as to the presence or not of a possible pathway for sensory impulses from the periphery of the limbs by way of the periarterial network and sympathetic chain. It is not our purpose to review the literature in detail but to quote papers germane to the subject and in which excellent reviews of the literature may be found.

Were the hypothesis true that pain may be carried centripetally by such paths, anatomically it should be possible to establish the presence of fibres passing the whole length of an artery to the periphery of a limb. Busch (1927) in experimental histological investigations has demonstrated that in animals no nerves, either medullated or non-medullated, travel along the entire course of an artery from the main trunk to its peripheral branches. He asserts that both types of nerve reach their area of distribution at the periphery via the peripheral nerve trunks, Coates (1932) in dissections of the human produced evidence that the limb arteries as they proceed distally receive frequent branches from the peripheral nerve trunks. The anatomical evidence thus favours the view that pain is unlikely to be transmitted along the periarterial network from the periphery.

These anatomical studies have received confirmation in the work of Woollard and Phillips (1932) as regards the efferent vaso-constrictor fibres. By anæsthetizing the various peripheral nerve trunks of the leg and arm these two investigators were able to establish that vaso-dilatation occurred in the distribution of the nerve. These observations suggest that the efferent nerves to blood-vessels utilize the peripheral nerve trunks to reach their area of distribution. Further, Davis and Pollock (1930), in an experimental study with decerebrate cats, were unable to provoke any reflex activity by the electrical stimulation of arteries of a limb which had its nerve supply sectioned immediately distal to the rami-communicantes. They believe that any afferent stimulus in such a sensitive reflex preparation as the decerebrate cat would have elicited a reflex response : and they conclude that their experiments substantiate the view that there is no long afferent pathway from the limbs which utilizes the periarterial plexus and sympathetic chain.

Foerster (1927), Foerster, Altenburger and Kroll (1929) have made many observations upon patients who had pathological lesions involving

various parts of the nervous system or who had had various surgical procedures carried out for the relief of pain. As the result of their intensive study, they deduced that the periarterial plexus may carry sensory stimuli from the periphery of a limb, and that the sympathetic chain may carry sensory impulses from the legs to enter the cord above the level of a spinal or root lesion. That their material was also pathological material renders the interpretation of the results obtained a task fraught with difficulty and some uncertainty.

The experiments recorded in this paper were carried out under physiological conditions, namely, no disease process was present, the subjects being healthy and the procedure was limited and exactly definable. It is our opinion that the described experiments are in accord with the anatomical evidence and favour the view that in man the periarterial plexus does not serve as an afferent pathway for pain from the periphery. It has thus been possible to establish that no pain impulses from the digits of the upper limb reach the central nervous system by passing along the periarterial nerves to the sympathetic ganglia, thence by the rami-communicantes to the posterior roots and so to the spinal cord.

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SHIVERING: A CLINICAL STUDY WITH ESPECIAL REFERENCES TO THE AFFERENT AND EFFERENT PATHWAYS.

BY V. UPRUS (TARTU), G. B. GAYLOR (GLASGOW),[1] AND E. ARNOLD CARMICHAEL.

SHIVERING may be caused by a variety of circumstances, different in kind and degree but productive of the same type of muscular activity. The various causes of these movements, generally regarded as shivering, are toxic as in the course of fevers, visceral as in relaxation of the sphincters, emotional as in fright and thermal as in disturbances of environmental temperature. This study concerns itself with shivering produced by alterations in temperature and was undertaken to investigate the pathways subserving the afferent and efferent sides of the shivering mechanism.

In a series of investigations on dogs, Sherrington (1924) found that, on transferring an animal from a hot to a cold atmosphere, shivering occurred. If the animal had a spinal transection, shivering occurred sooner than in the normal animal and was more profound. There was, however, no shivering below the level of the lesion. When the paraplegic part of the animal was immersed in cold water, there occurred shivering independent of sensory stimuli from the part immersed. The conclusions from Sherrington's work were that shivering produced by cooling an animal was the result of changes in blood temperature acting on a "centre" higher than the spinal level, or the result of such blood temperature changes acting upon sensory endings in the intact region of the body and the consequent stimulation of a "centre" higher than the spinal level.

Dworkin (1930) found that shivering may occur in acute preparations after transections of the brain stem had been made as low down as 2 mm. cephalic to the calamus scriptorius of rabbits.

Keller (1933) found that shivering occurred in cats even when

[1] This work was undertaken on behalf of the Medical Research Council at the Research Unit, National Hospital, Queen Square, London, while Dr. Uprus held a Rockefeller Foundation Fellowship and Dr. Gaylor a Halley-Stewart Research Fellowship.

transections of the medulla oblongata had been made. In the work of Penfield and Bazett (1924), shivering was not produced in chronic preparations of cats decerebrated at the level of the superior colliculi. It is difficult to make definite conclusions about work in acute and subacute preparations, but the general trend of this evidence points to existence of some cephalic "centre" necessary for the production of shivering.

Method.

Two series of studies were undertaken. A number of healthy men, chosen from a group of young post-graduates, were submitted to the following experimental procedure. The method employed was then adapted to the investigation of patients suffering from the effects of focal lesions of the central nervous system.

The subject was seated or lay in a semi-recumbent position with the whole body exposed to the surrounding air in a draught-free cubicle. Following a control period of twenty to thirty minutes, the legs were immersed up to the level of the tibial tuberosities in a tank of water kept at a temperature of 44° to 45° C. When adequate warming had taken place, as evidenced by general vaso-dilatation, increase of pulse-rate and frequently sweating, the legs were transferred as rapidly as possible to a tank of water kept at a constant temperature between 10° C. and 15° C. During the immersion in cold water, shivering manifested itself. The shivering, ushered in by a feeling of coldness and stiffness of the limbs, was permitted to continue until it was impossible to inhibit the clonic-like tremor by voluntarily relaxing or bracing the muscles. When the shivering had become uncontrollable, the legs were transferred to the tank of warm water until shivering ceased and peripheral vaso-dilatation had been initiated for a second time. At all times the water in the tanks was kept constantly circulating. During the course of the experiment the temperature of the skin at various sites on the body was frequently determined by means of thermocouples. A record of the rectal temperature was obtained by means of a special thermocouple inserted 5 to 6 cm. within the external sphincter.

The rectal thermocouple was of a particular type, designed to give rapid registration of temperature change. A hollow finger-like copper structure of low thermal capacity fixed to a vulcanite end grooved to permit the sphincter ani to close upon it, constituted the heat receptor from the rectal mucosa. Into the thin piece of copper were soldered two wires, one constantan and the other copper. In the rectal thermocouple a difference of potential proportional to the temperature of the

copper was measured against a constant difference of potential in a second thermocouple kept at constant temperature of 37° C. The difference between the currents in the two thermocouples was registered on a high sensitivity mirror galvanometer. By means of a factor determined by physical experiment and found to be constant over temperature variations such as were recorded, the amount of deflection above or below a zero mark was translated into terms of temperature in degrees centigrade and subtracted or added to 37° C. Thus the rectal temperature was obtained at any point of time. The limitations of this method are a necessary lag on the part of the rectal thermocouple in virtue of thermal capacity, and a small lag, of maximum twenty-two seconds, in the galvanometer itself. Although no claim is made that the rectal temperatures recorded here are absolute, it is certain that changes of temperature are registered with reasonable rapidity, as can be seen by many of the findings. The principle of skin temperature recording was the same, but the applicability of a thermocouple directly to the skin surface obviated the necessity of a large surface couple and in registration a needle galvanometer was found sufficient. Readings of rectal temperature were made every fifteen seconds and skin temperature readings at about the same intervals of time. Direct observation was made of the time of onset and cessation, the distribution, the intensity and the character of shivering. Notes were also made of sweating and "goose-skin" when they occurred. The subject at the commencement of the experiment was invited to co-operate by informing the observer of any subjective sensation of warmth or cold which might be experienced.

Observations.

A. Normal Individuals.

Experiments were carried out on healthy individuals. During the period of control the skin temperature fell, except in the experiments when the air of the cubicle was kept at 37° C. or over; the rectal temperature remained practically level, in some falling over a period of twenty minutes, not more than 0·02° C., or rising even a smaller amount. After immersion of the legs in warm water for a period of five to fifteen minutes the skin temperature rose. The rectal temperature also invariably rose and before the rapid rise in skin temperature. The amount of rise in rectal temperature varied considerably, the smallest being 0·25° C., and the greatest 0·80° C. Following the immersion of the legs in cold water, skin temperature rapidly fell to as low a level as or lower than at

the commencement of the experiment, except when the temperature of the air of the cubicle was kept high. When this was done little or no fall occurred in skin temperature, except when sweating had been present. The rectal temperature within one to three minutes following the transference of the legs to cold water commenced to fall rapidly. In two experiments a fall of 2·5° C. in rectal temperature occurred in twelve minutes: however, in the majority of individuals the registered fall

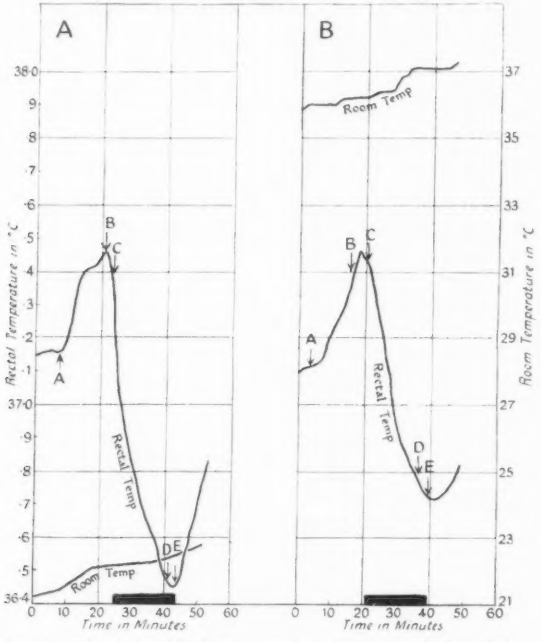

FIG. 1.—Normal. Chart A with low room temperature. A, legs into water at 45° C. B, legs into water at 9·1° C. C, commenced shivering. D, legs into water at 45·4° C. E, stopped shivering.

Chart B with high room temperature. A, legs into water at 45° C. B, legs into water at 12·1° C. C, commenced shivering. D, legs into water at 43·4° C. E, stopped shivering.

averaged between 1° and 1·50° C. in ten to twenty minutes. After immersing the legs in cold water and at the time when the rectal temperature was falling, shivering commenced. The subject first complained of a cold feeling or "as if inclined to shiver"; this was succeeded by obvious shivering, at first in irregular outbursts in varying muscle groups, which rapidly became more intense and widespread. In the early stages the shivering could be caused to disappear either by

voluntary bracing or relaxing the muscles. Eventually the shivering became so intense that no effort on the part of the subject could control it. When the shivering had become uncontrollable, the subject was still able to perform voluntary movements, though these were frequently interrupted by the involuntary shivering; thus acts of precision were performed with the greatest difficulty.

On the legs being removed from the cold bath and placed in warm water, the rectal temperature gradually altered its gradient of fall and then commenced to rise. Nearly co-incident with the cessation of the fall and the commencement of the rise of rectal temperature, shivering ceased. The end of shivering was seldom abrupt—generally it became less severe, less widespread, then in irregular bursts, finally to cease altogether. It was striking to observe during this period an apparent relaxation suddenly come over the subject, which in time was coincident with the commencement of the rise of rectal temperature. It thus appeared that shivering was closely connected with the fall in rectal temperature and was independent of alteration in skin temperature resulting from the vaso-constriction produced by immersion in cold water. To elucidate this aspect two subjects were submitted to the same procedure, only differing in that the air of the cubicle was kept at 37° C. (fig. 1). In this way an attempt was made to avoid cooling of the skin, but owing to eruption of sweat it was not possible to prevent a slight fall in skin temperature. In spite, however, of the almost negligible fall in skin temperature shivering occurred under these conditions in the two subjects, and in every way was similar to that produced when the air of the cubicle was at a lower temperature.

B. Subjects with Lesions of the Nervous System.

(i) *Complete transverse lesion of the cord.*—In two cases observations were made, but in only one was the rectal temperature of sufficient accuracy to be of value for full analysis. In the first case, in which rectal temperature readings were inadequate, it was noticed that no shivering occurred below the segmental level of the lesion though reflex activity was present. Shivering of the type seen in normal subjects only occurred in muscles innervated from above the segmental level of the lesion. In the second subject who had a fractured spine with loss of reflex activity below the level of the ninth dorsal segment on the left side and tenth dorsal segment on the right side, shivering occurred when the legs, after previous immersion in warm water, were immersed in cold water. Only those muscles having a nerve supply from the segments above the level

of the lesion showed the irregular movements of shivering. The onset of the shivering occurred during the fall of the rectal temperature at the tenth minute after immersion of the legs in cold water. Following the transference of the legs to warm water shivering ceased three

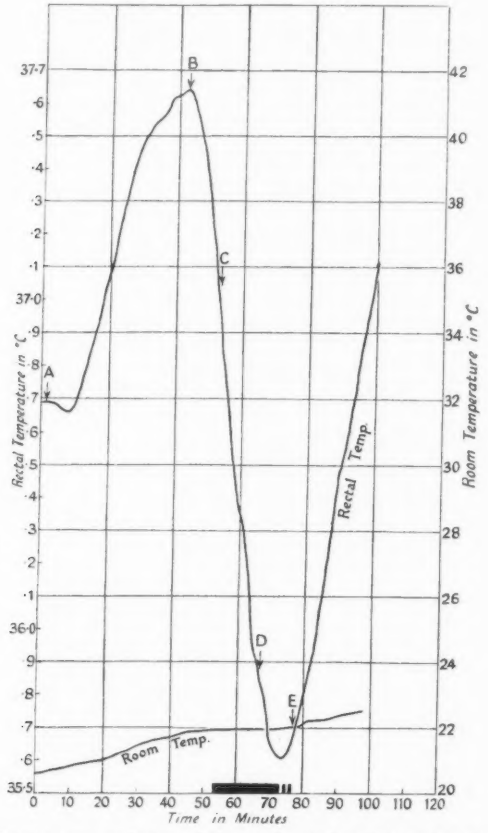

FIG. 2.—Complete transverse lesion of the cord. A, legs into water at 44·5° C. B, legs into water at 9·8° C. C, commenced shivering. D, legs into water at 44·4° C. E, stopped shivering.

minutes after the rectal temperature began to rise, though the actual rectal temperature was 0·99° C. below that registered during the control period when no shivering was manifest (fig. 2). It is of interest that before shivering was observed the subject complained of a cold subjective sensation in the upper part of the trunk.

From these two observations it is apparent that not only must the muscles in which shivering occurs have their motor innervation intact, but also that shivering as produced in these experiments is dependent upon a central mechanism at a higher level than the spinal segment. Further, these two experiments demonstrate that the shivering so produced is initiated not by sensory impulses passing centrally from the immersed limbs, but by cooled blood traversing the tissues above the level of the segmental lesion. In the discussion this will be more fully dealt with.

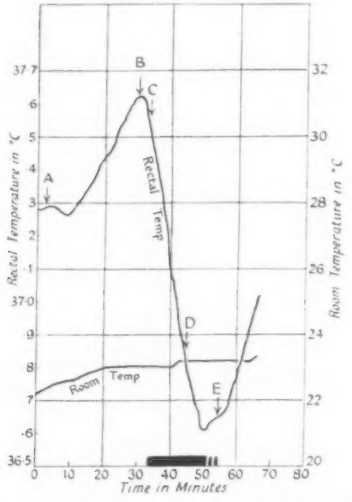

FIG. 3.—Hemiplegia. A, legs into water at 45·2° C. B, legs into water at 9·8° C. C, commenced shivering. D, legs into water at 44·2° C. E, stopped shivering.

(ii) *Lesions involving the pyramidal tract in the cerebral hemisphere.*—Five subjects were studied. The degree of motor involvement varied from a slight paresis to a marked weakness with great spasticity. In all, some voluntary movement remained. It was possible to produce shivering in the muscles of both the healthy and paretic side of the body in all subjects. The shivering had the same relationship to the fall of rectal temperature, and ceased in the same manner when the rectal temperature commenced to rise, as in normal subjects (fig. 3). In two subjects the shivering manifested itself first on the hemiplegic side, but in the remainder it commenced either on the sound side or on both sides at the same time. Coincident with, but sometimes preceding the

shivering, the hemiplegic limbs became more rigid, the upper limb contracting so as to become flexed and adducted.

The study of these cases demonstrated conclusively that damage to the pyramidal tract in no significant way influenced the character, time of onset, or cessation of shivering. These experiments did not offer conclusive proof that the mechanism of shivering was independent of the pyramidal tract as in all subjects there remained some degree of voluntary movement. It appeared unlikely, however, that the pyramidal pathway was necessary as the degree of hemiplegia did not influence in any way the character of the shivering or its temporal relationship to the rectal temperature.

(iii) *Lesions involving the thalamus.*—In subjects suffering from symptoms and signs referable to a lesion in the region of the thalamus, no demonstrable difference occurred in the time of onset and cessation, the distribution or intensity of shivering on the two sides of the body.

It becomes evident that loss of conscious sensation from one half of the body does not influence the mechanism associated with shivering.

(iv) *Lesion of the cerebellum and cerebellar pathways.*—The lesion in one case investigated was, so far as could be determined clinically, as purely cerebellar as possible. A long history of years of incoordination was present and the case presented the features of a primary atrophic lesion of the cerebellum and its connections. By the method described, shivering was produced which in time of onset and cessation, severity and distribution, was the same as in normal individuals. The relationship between these events and the rectal temperature was in essence similar to that found in the normal condition. A remarkable phenomenon was observed in this case, in that although shivering occurred the movements were modified from the clonic-like type to choreiform movements. In another case with a unilateral lesion of the cerebellum the temporal relationship of the shivering and rectal temperature were identical, and on the side of the lesion the shivering was of a choreiform type.

An intact cerebellum appears a necessary requirement for the production of the clonic-like movements of shivering.

(v) *Bilateral cordotomy.*—A subject who had been operated on two years previously was investigated. The spino-thalamic tract on the left side was cut at the third dorsal segment and on the right side at the fifth dorsal segment. The subject had a complete sensory loss to pin-prick, heat and cold up to the segmental levels incised. The deep reflexes in the legs were brisk and the plantar responses were extensor.

The subject, however, had excellent control of his legs and was able to walk several miles a day without the aid of support. In this particular subject, shivering was induced with ease, the period of latency between cold immersion and the onset of shivering being very short (fig. 4). Shivering was limited to the muscles innervated from segments above the level of the incisions in the cord. Even with profound lowering of

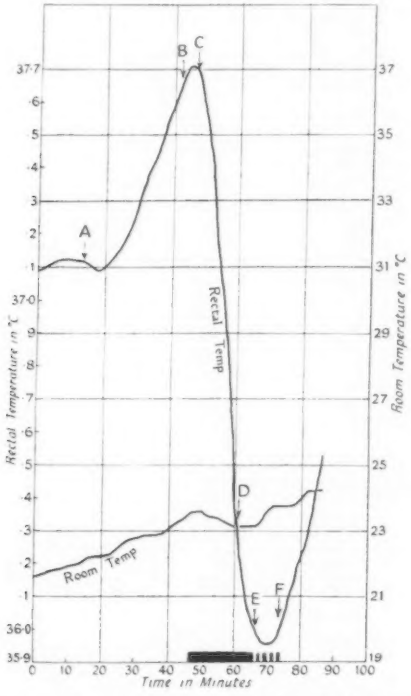

FIG. 4.—Cordotomy. A, legs into water at 45° C. B, legs into water at 10·6° C. C, commenced shivering. D, legs into water at 45° C. E, relaxation observed. F, stopped shivering.

rectal temperature it was not possible to induce shivering in the muscles innervated from segments below the incisions in the cord.

This case demonstrates that in the presence of slight dysfunction of the pyramidal tract shivering does not occur. By [deduction it would appear relevant to suggest that the efferent mechanism of shivering is dependent upon the integrity of tracts lying in close approximation to the spino-thalamic such as the tecto-spinal and rubro-spinal.

Discussion.

In these experiments rectal temperatures were recorded at a distance of 5 cm. from the sphincter. While it is impossible to state categorically that the temperature at such a level is that of the circulating arterial blood, it is unlikely that it can be otherwise. Consequently for the purpose of the discussion the rectal temperature recorded has been accepted as indicating the arterial blood temperature and will in the discussion be referred to as the blood temperature.

From the investigation of normal subjects, the constancy of production of shivering during a phase of rapid fall in blood temperature suggested that in normal shivering changes in blood temperature might be of significance. Two positive findings were of constant occurrence: first, the period of latency between the application of the sensory stimulus of cold to the immersed limbs and the onset of shivering; second, the cessation of shivering near the lowest point on the blood temperature curve which occurred sometime after the legs had been immersed in warm water. Only in one instance did shivering cease at the point of transference of the lower limbs from cold to hot water. The period of latency between cold immersion and commencement of shivering is against the view that the mechanism of shivering is entirely reflex unless summation of stimuli is invoked to explain the occurrence.

The type of shivering produced in these investigations of normal people ceased after the limbs had been heated for some time but not before there was some definite alteration in the rate of fall of blood temperature or a definite rise. This fact was again suggestive of the possibility that blood temperature played an important part in the causation of shivering. It must be made quite clear that the mechanism producing shivering as described above is the only mechanism under present consideration. It is known that the shivering of febrile conditions occurs with a rising internal temperature—an observation which was confirmed in the present series of studies by making a continuous record of rectal temperature during a malarial rigor. This mechanism is probably of a different character although objectively there appears to be no difference in type of movement. Again the sensory function as productive of shivering is admitted; an immediate and transient response to an extreme but indifferent thermal stimulus is characteristic of well-established reflex activity operated without change in blood temperature. It is unlikely that such immediate but transitory shivering as occurs on

immersion in a hot or cold bath can be brought about by a change in blood temperature.

The proof that change of blood temperature may cause shivering lies in the investigation of paraplegic patients. In these cases no possible sensation travelled up from the legs. Further the sympathetic chain may be excluded as being a possible afferent pathway. The only mechanism whereby shivering was produced depended therefore on some alteration in the state of circulating blood. There is no evidence to suggest that this alteration was of a chemical nature and the fall in internal temperature was so striking and so constantly associated with shivering that it was believed to be the causative factor.

If a fall in blood temperature is the effective stimulus to such shivering as was produced here, a consideration of the possible sites of action has to be undertaken. These possible sites are: (1) Directly on muscle; (2) directly on spinal segments; (3) on temperature endings originating impulses to be conveyed to a "centre"; or (4) a "centre" itself without an afferent nervous pathway.

The first and second possibilities are excluded by the fact that paraplegics do not shiver below the level of the lesion. The impulse to shiver must be dependent upon a mechanism higher than the spinal level, and shivering is not an intrinsic response of muscle to cooling blood.

There remain two ways in which such a falling blood temperature may act through the medium of the nervous system: (*a*) On a centre in the brain sensitive to temperature change; (*b*) on thermal endings remaining in communication with the entire nervous system.

The proof of either hypothesis was beyond the limitations of the material at our disposal. The following fact, however, may be of importance. It was easy to make the case of cordotomy shiver above the sensory levels. If the skin endings were in reality the afferent end of a reflex pathway, the motor expression of which was shivering, it is natural to assume that the greater the area of intact skin the easier it is to make the individual shiver. In the case of the patient with cordotomy, the intact skin area was confined to the head, neck, arms and shoulder girdle regions, but he shivered as readily and as intensely as did the normal individual. This piece of evidence is against the second hypothesis. The same argument holds as evidence against endings in situations other than in the skin being the effective afferent end of the shivering arc. If the direct stimulation of a "centre" cannot be admitted, then a separate thermal receptor in the brain or in a situation

unaffected by any of the lesions in the present series, has to be postulated. In spite of the doubt about the exact nature and site of operation of the effective affector stimulus, the existence of a "centre" higher than the spinal level must be inferred. No attempt is made to localize that "centre" directly because we have no evidence pointing to its primary involvement. Certain deductions may be made by argument from the results obtained.

Shivering occurs on both sides when the pyramidal tract has suffered insult. The amount of shivering in respect of excursion of the tremor is, if anything, a little greater on the hemiplegic side. Shivering occurs apart from pyramidal tract integrity. Shivering in a patient with cerebellar disease is strikingly modified to a choreiform tremor. It is natural to conclude that such a modification indicates some dependence of normal shivering upon intact cerebellar pathways.

In one case there was a lesion of the thalamus; the localisation of the lesion was confirmed by X-rays which showed a calcified mass in the right thalamus. When this patient was made to shiver there was no deviation from normal appearances and there was no difference between the tremor on either side. The further observations on hemiplegic patients with definite thalamic signs showed normal shivering to the usual stimuli. These findings point to the shivering mechanism being independent of the thalamus.

Most instructive is the case of cordotomy in which there was no shivering below the level of the lesion. In this case the absence of shivering must be due to interruption of spinal pathways. Physical examination revealed that there was interruption of the spinothalamic pathways and some interference with extrapyramidal tract conduction.

Absence of shivering cannot be accounted for by the interruption of spinothalamic pathways since there is no deviation from normality so far as shivering is concerned when there is thalamic disease. The slight interference with pyramidal path conduction is not adequate as an explanation because it has been shown that shivering occurs when the pyramidal pathways have been interrupted.

Interference with cerebellar pathways cannot be held responsible because there was no shivering, whereas it has been seen that shivering of an abnormal type occurred when the cerebellum itself was diseased. The only pathways left to consider are the extrapyramidal such as the tectospinal and rubrospinal. These tracts descend in the spinal cord in areas which would be sectioned by cordotomy. We may, therefore, conclude that they constitute the pathway by which the impulses of

shivering (originated in the brain-stem either directly or indirectly by the falling blood temperature) reach the muscles.

SUMMARY.

A method is described of inducing shivering constantly in normal subjects.

The relationship between the onset and cessation of shivering to rectal temperature change is discussed.

Cases with manifest disease of the central nervous system were made to shiver and the responses observed.

From the investigations it has been shown that shivering, as produced by the constant method described, is independent of pyramidal thalamic and cerebellar integrity, although the type of tremor produced is modified by cerebellar dysfunction.

The conclusion is reached that the effective stimulus is a falling blood temperature acting directly on a "centre" or on a thermosensory mechanism capable of stimulating the shivering "centre." The downward pathway from the "centre" is by exclusion shown to be an extrapyramidal pathway, either the tectospinal or rubrospinal.

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NOTE ON THE NATURE OF THE MOTOR DISCHARGE IN SHIVERING.

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THE rapid fluctuations in the muscular contractions of shivering appear to the eye to vary in speed from relatively slow contractions to rapidly repeated shaking closely resembling the clonus of spastic muscles. The character of the movement changes from time to time and from place to place in the limbs. To seek more closely for any relationship between the character, location and intensity of the movements in different regions we have recorded them from jaw, thorax, biceps brachii, and quadriceps femoris, concurrently. For this purpose a small light balloon was attached between the teeth, others over the belly of biceps brachii and quadriceps, where they were held by a piece of adhesive strapping to the skin over the remaining belly of the muscle, and a band around the thorax at the level of the nipples compressed also a further balloon. The pressure within each balloon was registered optically by manometer and mirror and recorded on a moving strip of bromide paper. In three experiments the action currents of biceps brachii or quadriceps were also registered on the same strip of paper. Shivering was induced by rapidly cooling the right upper and lower limbs by ice water after the subject had been warmed until sweating had occurred. The left limbs, from which the records were made, were rested in a natural posture of semi-flexion.

As the body temperature falls the first indication of onset of shivering was usually an isolated twitch of the masseter, on one occasion of the whole thorax. This preliminary twitch is followed by others at very variable intervals of 0·2 seconds to 1·6 seconds. The first onset may be a small series of three or four twitches rapidly repeated. If the shivering be gradual in onset, presumably from slower fall of temperature,

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these single twitches occur in one muscle or another for many seconds before the next change occurs. In one or other muscle, usually first in the masseter, series of such twitches are repeated rapidly at rates from 4 to 6 a second for a period and such bouts of clonic twitching then gradually increase in length (figs. 1 and 2). At this time the twitching in the upper and lower limb continues to be single or in sparse groups (fig. 1). The shivering at this and later stages can be caused to cease immediately in any particular muscular group by voluntary contraction of that group (figs. 1, 2 and 3). It can also be ceased by voluntary restraint, not necessarily but usually with some slight bracing of some part of the body and cessation of respiration (fig. 3). Passive movement of a limb lessens the movements of that limb, but complete voluntary relaxation is difficult if not impossible to maintain during this procedure.

As the twitching becomes fused into clonic outbursts in each muscular group the respiration becomes irregular, with periods of apnœa. At this time one or other muscle may still continue twitching.

The intensity of shivering in any particular muscle group, together with the time of onset of shivering, appear to be related mainly to the amount of other contraction present. A muscle completely at rest shows early twitching and early fusion of twitches. A maintained posture, however slight, delays the onset of shivering.

A voluntary movement in the more intense stages of shivering is followed by greater outburst of shivering in the muscles concerned (figs. 2 and 3). Similarly a deep breath is accompanied by partial or complete subsidence, and followed by increased shivering for an interval (fig. 4). As the intensity increases the respiration deepens and the periods of apnœa lessen so that regular breathing is reasserted. The periods of clonic twitching increase in length, and the intervals shorten, until one or other muscle commences continual repetitive clonic movements at the rate of 4 to 6 a second (fig. 3).

The twitching, and the periods of rapidly repeated clonic contraction are not coincident in time in any two of the sites examined. The rate of rapid beating varies from time to time in any one muscle group, and when two are beating concurrently there is no correspondence in their rates (figs. 5, 6, 7 and 9). The smaller muscles usually contract more rapidly, and movements at the hip and shoulder are slightly slower than in the jaw or distal joints of the limbs. When recovery occurs after the voluntary suppression of severe shivering the commencement of the clonic movement is also independent in each muscle, both in time and in frequency (fig. 9). When all the musculature is affected, however,

there occur intervals when the clonus of many muscular groups becomes synchronous for periods of at first one or two seconds and later for longer. This appears to be the maximum development of shivering, a "shuddering" movement of the trunk and limbs. It will be observed, however, that even here some groups, for example, the closing muscles of the jaw in fig. 6, remain independent in rhythm. At this stage the subject has the greatest difficulty in abolishing the movement by effort of will. Richet [2], in discussing the maximal rate of repetition contraction in muscle, stated that the rate of tremor in shivering was about 10 to 11 beats a second, and did not exceed 13 a second. We have not encountered rates as high as this, slightly over 6 beats a second being the highest observed frequency.

The action currents of shivering movement, as recorded by a Matthews oscillograph, reveal single diphasic waves for many of the first twitches, with the early appearance of small groups, in some of which identical wave forms are repeated at intervals of one-twenty-fifth second, suggesting that the slightly longer twitches are small tetanic contractions. These become brief tetani of three-fifths second to one second duration. For long intervals the discharge may now become sparse but regular, as in slight postural tone. Gaps in this discharge corresponding to the beats of concurrent clonic contraction in other muscles occur only when the generalized shudder occurs (fig. 7). Sooner or later the action currents become grouped into dense volleys separated by quiet intervals, corresponding to the regular alternation of the clonic beats (fig. 6). In each such beat complete fusion of the action currents into one large electrical variation was not at any time seen, a feature which is in sharp contrast to the electromyogram of the reflex clonus of spastic muscles. The general appearance of each outburst in any one muscle in shivering suggests strongly that there is rapidly repetitive discharge in each motor unit for each beat, rather than that single impulses in each fibre group were out of phase in each volley as in reflex clonus.

We have recorded reflex clonus in the lower limb of two patients suffering from a spastic paraplegia, concurrently with the outbursts of shivering in the upper limb and mandible. We were unable to demonstrate any interruption or change in type of the clonus in the lower limb. Voluntary contraction converts the clonic discharge of shivering into a continuous one, without any stage in which the voluntary contraction itself becomes clonic, as occurs in the presence of reflex clonus. The clonus of shivering and that resulting from damage to the pyramidal

tract differ, therefore, not only in the nature of discharge, but in relationship to cold and to voluntary movement.

The suppression of shivering by voluntary effort is not always accompanied by contraction in the shivering muscle, and the action currents may cease completely as in fig. 8. The subject feels that he achieves the cessation by a general relaxation, and the effect may be purely inhibitory. Nevertheless, cessation of respiration occurs, and this probably indicates some contraction of the musculature of the trunk.

The myographic characteristics of the type of shivering brought about by rapid cooling of the skin surface, therefore indicate a movement which has independant development in each muscular group concerned. This independance affects both the manner and the time of development, and would suggest a local segmental mechanism for its production. The experimental investigations of Sherrington [3] have demonstrated the limitation of shivering to the headward segments of the dog with spinal transection, both in response to lowered blood temperature and to direct cooling of the skin of the segments concerned. Our experience with patients suffering from transverse lesions of the spinal cord has also convinced us that the central control of shivering is cephalic. The movements of the panniculus resembling shivering which were reported by Goltz [1] to occur in the isolated segments of the spinal animal in response to direct stimulation of the skin by cold, have not been obtained by others [2, 3] despite careful research. There therefore appears to be no basis for the assumption that shivering can occur as a segmental spinal reflex. At a stage of high intensity the rhythm of shivering becomes identical in almost the whole musculature, and this "shuddering" necessitates the presence of a co-ordinating mechanism to secure the identity of the rhythm in widely-spaced parts. The independent manner in which the movement develops in each muscular group therefore has more probable explanation in the varying states of the spinal motoneurones brought about by voluntary and postural factors, and affecting at each the manner in which discharge occurs in response to one cephalic nervous mechanism. Just as a strained posture of a limb results in delay in the appearance of the movement in that limb, so slight differences in posture combine with the discharge of shivering so as to alter its rhythm. This change of rhythm does not occur to any obvious degree with reflex clonus in spastic muscles, but we maintain that shivering is a separate and distinct repetitive movement. The manner in which shivering gives way to

voluntary movement allows it to fulfil the requirements of promotion of metabolism without the necessity for particular posture or interference with willed effort.

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DESCRIPTION OF PLATE.

Myographic Records of Shivering from the Normal Subject.

All figures read from left to right.

Fig. 1.—Shortly after the commencement of shivering, showing movements of the thorax (R), of closure of mandible (M), and of contraction of quadriceps extensor (Q). The twitching has already fused into small series in the mandible, while more isolated twitching is still occurring in quadriceps. Between *a* and *b* the subject clenches the jaw voluntarily. The time marking for such record has been stressed by a small black vertical line above the record at one second intervals.

Fig. 2.—As fig. 1, thirty seconds later, showing periodic apnœa and more continuous series of clonic twitching in the jaw. From *a* to *b* the knee was extended voluntarily to order.

Fig. 3.—As figs. 1 and 2, thirty seconds later. Quadriceps now shows continuous fine clonus. From *a* to *b* the knee was extended voluntarily, and from *c* to *d* the subject suppressed shivering by voluntary effort.

Fig. 4.—More rapid speed of recording. A vertical white line marks each one-fifth second. The broad dark horizontal line is the record of a Matthews oscillograph, recording action currents from quadriceps. At the commencement of the record the subject has just made an involuntary deep inspiration and as the respiratory recorder (R) returns to the record, the movements in the mandible (M) increase in amplitude, and a prolonged outburst commences at *a* two seconds later in biceps (B), with some clonic movement at the same rate in the pectoral muscles, seen as an alteration in the record from the thorax (R). The movement in the mandible ceases at *b*. At *c* a series of action currents in quadriceps extensor results from voluntary contraction. Their continuity is not affected by the rhythm of contraction in biceps at *d*.

Fig. 5.—As fig. 4. An outburst of shivering in biceps (B) and pectorals (R) occurs during a slower rhythm of flexion at the hip (Q) which was recorded indirectly by the balloon over quadriceps. There is no contraction at this time in quadriceps.

Fig. 6.—Record as fig. 4. Showing the electromyogram of clonic discharge in quadriceps with independent outbursts in the mandible (M) and biceps (B), with coincidence of the rhythm in biceps, pectorals and quadriceps from *a* to *b* with general "shuddering."

Fig. 7.—Records as fig. 4. Showing a more tonic type of contraction in quadriceps (Q), with some grouping corresponding to an outburst in biceps brachii between *a* and *b*.

Fig. 8.—Records as fig. 4. Voluntary suppression of discharge commencing at *a*.

Fig. 9.—During the recommencement of discharge ten seconds after fig. 8.

THE DISSOCIATION OF CORTICAL EXCITATION FROM CORTICAL INHIBITION BY PYRAMID SECTION, AND THE SYNDROME OF THAT LESION IN THE CAT.

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EXPERIMENTS on the motor cortex, such as stimulation or ablation, have commonly been interpreted in terms only of excitation or destruction of the cortico-spinal neuron. This practice Dusser de Barenne's (1934) recent work on laminar thermo-coagulation of the cortex seems to justify. Yet clinical neurology has persistently emphasized differences between the effects of cortical lesion and lesion of the cortical projection paths. True, these are more clear-cut on the sensory side than on the motor in the discrepancy between the thalamic syndrome and that of the somæsthetic cortex. Yet even on the motor side cortical and subcortical lesions, both involving the pyramidal tract, are certainly not equivalent. Nor is this to be expected. Obviously the cortical lesion entails destruction of a multitude of longer and shorter association neurons, together with the projection neurons. Moreover, the projection neurons are by no means a single tract, as Poliak's (1932) recent studies again show, but have supra-segmental as well as segmental destinations. Furthermore, the Betz cell neuron is not itself a simple cortico-spinal neuron, but a complex structure sending off collaterals at the level of the pons and perhaps into the corpus striatum. According as a lesion of the pyramidal system destroyed such pre-spinal projection neurons and collaterals or left them intact, its effects might well differ. With these considerations in mind the present research was designed, first, to evaluate the consequences of lesions of the pyramidal tract below its last large supra-segmental connection to the pons, and then to determine the activity of still surviving supra-segmental projection neurons and cortico-spinal collaterals by comparison of the effects thus produced with the familiar results of a cortical lesion, and by electrical stimulation of the motor cortex after degeneration of its segmental projection tract.

MATERIAL—PROCEDURES.

Ten adult cats in which the right pyramid had been cut at the level of the trapezoid body provided the material for study. Under

ether anæsthesia a ventral approach along the lateral wall of the pharynx exposed the occipital bone between the bullæ tympani and the edge of the foramen magnum. Through a hole in this bone, 8 or 10 mm. long and half as wide, the dura and pia were slit, the basilar artery retracted to the left, and a fine knife inserted exactly in the mid-line, at the mid-level of the trapezoid body and to the estimated depth of the pyramids. The cutting edge was then rotated to face the right pyramid, and the lesion made by drawing the knife upward in an arc to its lateral edge, visible as a deeply marked groove containing a small vein. To ensure the completeness of the lesion, the knife was then inserted at this lateral border and swept over to the mid-line. The operation was virtually bloodless at all stages. The animals made a remarkable recovery, showing neither shock nor excessive excitement. In an hour or less they could run and jump and behaved, except for the specific effects of the lesion, as any cat subjected to anæsthesia for forty minutes. The only post-operative complication was a transitory difficulty in swallowing.

Of the series of 10 cats 5 were killed at three weeks, 3 in the sixth month and 2 at the end of a year. Four of these last 5 were subjected to secondary ablations of the motor cortex of one side some time before death. In all the animals but one the motor cortex of each side was thoroughly explored electrically either just prior to ablation or to death, or at both times. After death by ether the vascular system was flushed with salt solution and the material fixed by the intra-aortic injection of Müller's fluid. The brain and cord were removed to Müller's fluid and later examined by the Marchi or Pal-Weigert method as required.

Examination of the brains before removing the specimens showed that all the lesions had been correctly placed over the trapezoid body and had completely severed the right pyramid without injuring the left. In one animal the brain had herniated into the bone defect. With lesions of months' standing the right pyramid was reduced to a flat strand below, while the left remained of normal size unless the left motor cortex had also been removed. The shrinkage following cortical ablation did not, however, in any case equal that resulting from the lower lesion.

Observations on the Living Animals.

The functional deficit of pyramid section.—One description will suffice for the series of cats, for with one exception all elements of the syndrome were demonstrable in every animal at all times, from two

hours after the operation throughout the survival period, even to a year. The effects of the lesion were appreciable only in the contralateral limbs, the axial musculature escaping except for a transitory deviation of the tail to the normal side. Homolateral symptoms were totally wanting. The lesion disturbed the normal balance of flexion and extension in progression, the fore and hind extremities being used stiffly with little or none of the characteristic triple flexion. Consequently the animals limped, for a time the toes on the side of lesion dragged, and either as an integral result or in compensation a circumduction of the hind developed, resembling that of a hemiplegic man. In running and jumping the stiffness was frequently so great as to throw the animal towards the normal side. Accompanying this stiffness was weakness, unmistakable during the first few days as a tendency for the affected limbs to give way as the body's weight came to rest on them; and later, apparent only as the animals stood at rest, in a "knuckling under," as it were, of the fore-leg at the wrist, suggesting imperfect fixation at this joint.

Corresponding defects appeared in posture. A normal cat held in the air by head and tail extends all four extremities, or when suspended by the hind or fore legs it extends those left free. The cats with unilateral pyramid lesions likewise extended the free legs equally on the two sides. But given support for the back, or when held in the air somewhat longer, flexion supervened in normal limbs, while those affected by the lesion remained extended. This occurred too when the animals were slung in a hammock in the upright position, the legs being thrust through holes. Extensions was often retained even when the animal had begun to climb out, a procedure invariably initiated by the limbs of the normal side.

With the cat lying quietly supine on lap or table this sequence was again repeated; an extension, initially symmetrical, became asymmetrical through flexion of the normal legs. From a few seconds to as long as ten minutes were required for the difference to mature, and the quieter the animal the slower its development. In this posture in which the animals were comfortable, a feature of the maintained extension was its passive quality, which was obscured by the tenseness of animals held in the air. The flexion of the normal legs was active immediately prefacing an attempt at righting or in general preparedness. These extremities opposed a correspondingly great resistance to passive extension while co-operating in flexion. In contrast, the behaviour of the affected legs was almost neutral, neither flexion nor extension being much resisted, and flexion, once passively imposed, was commonly

retained. The apparent hyper-extension of the crossed limbs thus appears as a normal extension abnormally prolonged because of a deficiency in flexor activity.

In postural reactions in the more precise sense, as studied by Magnus, Rademaker and others, the selectivity of the defect for certain flexor activities was again exhibited. For example, in the "Sprungbereitshaft" of Magnus the downward thrust of the legs of an animal dropped suddenly through space was executed equally on the two sides in the presence of unilateral pyramid section, but the flexion which terminates this extension if the descent be halted in mid-air was lacking in the crossed limbs. Again, as an animal was slowly lifted from a surface, a leg lacking cortico-spinal innervation lost contact first, not from any deficiency of extension, which was symmetrical, but because certain small movements which operate continually to keep the normal foot in the best position for contact were wanting. The larger flexion which follows in a normal leg when contact is finally broken, and which is sometimes clearly aimed at placing the foot on the nearest object, was also wanting.

Analysis of the defect in these two instances brings clearly into view what was suspected in the initial study of posture and gait. The basic postural mechanism of extension is intact, symmetrical and not over-active, but a large group of preparatory and terminal movements, movements of adjustment and correction, largely flexion, are diminished or wanting. The absence of these produces the abnormalities of posture. These movements all partake of the nature of placing reactions. Further study was pursued along the lines laid down by Bard (1933), and his analysis of the cortical control of the placing and hopping reactions was used as a standard against which to assess the effects of subcortical lesions on the same mechanism.

Of the five placing reactions described by Bard, only four were examined in the presence of pyramidal lesions. These were: (1) Placing of the feet in response to contact of the dorsum of each with a table edge; (2) replacing the fore or hind feet after they have been thrust over a table edge; (3) replacement of a leg passively abducted; and (4) placing of the fore-feet on the edge of a table when the chin of the animal is brought to rest upon it. The fifth reaction, placing in response to stimulation of vibrissæ, which necessitates the enucleation of the eyes, was omitted in favour of the visual placing reaction described by Bard and Orias (1933). The hopping reactions were also studied; these were elicited by horizontal displacements of the animal's body.

through space, either backward or forward or from side to side, as corrective movements to keep the extremities which must be in contact with the table directly under the body.

Before proceeding to describe the deficiency in these reactions following pyramid lesions, it may be pointed out that the first three placing reactions and the hopping reaction are elicited by stimuli from below the level of the lesion, and largely from the leg concerned. The chin-on-table reaction and visual placing, on the other hand, originate above the level of the lesion. Hence, inadvertent sensory destruction, in particular of the medial lemniscus, may interfere with the former reactions, but not with the latter.

In this study, as in Bard's, defect in the placing reactions appeared first as clumsiness of gait and oddities of posture. In running the paws turned under, or the legs slipped to the side, front or back. In standing or sitting the legs likewise slid out of position, the fore and hind limbs often scissoring. Such abnormalities were uncorrected. Examination of the special placing reactions showed that the entire group was gravely impaired. The first reaction, that to contact of the dorsum of the paw with table edge or finger, suffered most, being virtually extinguished. If, however, a proprioceptive stimulus were added to the tactile, by moving the animal horizontally to the table until the extended limb was passively displaced, a reluctant placing could generally be obtained, at least after the first days. The amount of passive displacement required (measured with a protractor) decreased progressively during the first month or two, and in one animal up to the fourth month after operation. But finally a threshold was established, between 20° and 60°, which remained fairly constant for each animal under standard conditions of examinations (animal quiet, unfatigued, in good health, and weather not too hot). This represents the only quantitative data on recovery obtainable in these experiments. The remaining three cutaneous-proprioceptive placing reactions had to be recorded only as present or absent. Under the so-called standard conditions of examination they were almost invariably absent, the chin-on-table reaction equally with those originating in the limbs. After the first week or so, by making the animal angry or excited, all three reactions could be brought out, though always sluggishly and clumsily compared with the normal. Fear, on the contrary, suppressed these reactions, even in normal animals.

The hopping reactions followed the course just described in that after a brief period of complete depression they made a variable, and indeed,

somewhat better recovery. After a time, usually a month or two, their condition became stationary with a result which differed from animal to animal, chiefly owing to differences in temperament. At best the recovery was imperfect, wide and uneven spacing of the steps remaining as permanent evidence of the lesion. Moreover, this recovery was not stable, for hot weather, illness or subsequent operation immediately brought about a return to the previous state.

The condition of visual placing presents an interesting problem, for, as Bard and Orias (1933) have shown, this reaction survives ablation of the sensorimotor cortex and is abolished by removal of the area striata. Section of the pyramid greatly reduced it. Indeed, with both fore-legs free the normal only was placed. Only if the normal limb was restrained, or the animal excited and eager to escape to the table, was the leg affected by the lesion brought into play. This effect of the lesion on a reaction using corticifugal pathways other than those from the motor area does not, however, necessarily reopen the question of the origin of the pyramidal tract, which Holmes' and May's (1909) Nissl studies, on cats among other animals, showed to be co-extensive with Betz cell distribution in the cortex. The effect of the lesion on the excitability of spinal centres, which will be analysed later, offers a simpler explanation of this result.

Examination of placing and hopping does not, however, exhaust the functional defect from pyramid lesions in cats. There remains a general deficiency of usage of the limbs quite outside these reactions, the full extent of which has probably gone unappreciated, but which was unmistakable in the animals' two most characteristic activities, namely, pawing induced by curiosity and the clawing of anger. Both these activities were permanently diminished on the side opposite the lesion. Indeed, when both legs were free, the preferential use of the normal was so great that only excitement brought the other into play. Then, however, its execution was indistinguishable from the normal. In this general deficiency of usage the flexor and extensor elements in movement suffered together, though not equally.

Such further consideration of the effects of a pyramidal lesion in terms of defective or lost unit reactions still fails, however, to reveal one common aspect of the movements effected which the condition of the scratch reflex immediately after operation brought into sharp relief. One animal showed this especially well. She had an ulcer behind the left ear and prior to operation scratched it freely using the left hind-leg. When this was attempted after operation, the leg was brought up into

the extended position well if somewhat stiffly, but the series of alternate flexions and extensions which would have effected the scratch presented difficulty. In several trials nothing but the most trifling flexion could be attained. Finally, after the right hind-leg had been requisitioned without relief, the first three or four movements were executed, and thereafter the series followed with increasing ease and range. Clearly, the postural element of the reflex was intact, and only its phasic element impaired. This is true of other movements, for, whether in gait or in placing or hopping reactions, or in the more complex activities of pawing and clawing, the movement lost is phasic in character. The tonic or postural activities survive, neither impaired nor exaggerated, but apparently quite normal.

That the results of pyramid lesion are not complete, but partial loss of function should now be clear. In the case of the scratch reflex, just cited, the phasic movements were finally executed when relief was not obtainable in any other way. Likewise, in placing and hopping, pawing and clawing, if the stimulus were of sufficient intensity or imposed upon a background of sufficient general excitation the reaction followed. Conversely, general depressing factors, such as illness or hot weather as well as the specific inhibition of fear, suppressed all the reactions under consideration, even on the normal side. Whether a given reaction was obtained or not became in final analysis a matter of summation of excitation and inhibition at the final neuron.

The attempt will now be made to analyse the effects of unilateral pyramid section at this level. One set of reactions was particularly useful in this analysis. This was the reflex flexion which a normal cat gives as threshold response to pricking a paw pad or pinching the tips of the toes, which is attended in the fore-legs by blinking of the eyes. Severing one pyramid permanently increased the strength of stimulus required for the flexor response on the opposite side. Indeed, this was the most stable sequel of the lesion. However, the operation spared the cortical facial innervation, and conserved the normal low threshold for blinking on stimulation of either fore-paw, although with this strength of stimulation only the normal leg flexed. Certainly no sensory defect is involved here. The only interpretation is that the flexion reflex, the archtype of spinal reflexes, is normally under reinforcement from the cortex. In the words of the Sherrington school the cortex, via the pyramidal system, contributes to the central excitatory state of the flexor motoneuron pool, probably continuously, but perhaps only at the moment of elicitation of the reflex. By this much the excitatory state which must

be built up by incoming volleys of sensory impulses is diminished and threshold held low. Pyramidal lesions, by eliminating the first source of excitation on the opposite side necessarily increased the amount of afferent stimulation required for the reflex. Comparison of the myotatic reflexes of flexor muscles on the two sides showed a like inequality of threshold. The widespread flexor and abductor responses obtained bilaterally from a single stimulus, as percussion over the sacral spines, were commonly weaker on the side affected by the lesion. Clearly, then, the spinal flexor mechanism had suffered a general loss of excitation which impaired any action utilising it.

This effect of pyramidal lesion on the flexor centres of the cat's cord is obviously commensurate with the large flexor representation in the cat's cortex, as revealed by electrical stimulation. Similarly, then, the spinal extensor centres might be expected to suffer a small loss of excitation in proportion to the meagre cortical representation of extension. This was not demonstrable. To casual inspection indeed, the contrary condition of increased excitability seemed to result. But the hyperextension pervading movement and posture has already been resolved into an ordinary degree of extension, inordinately maintained. The lack of excessive rigidity in this extension, as gauged by the resistance opposed to passive flexion, has been pointed out.

No good superficial extensor reflex could be found for study, and even the myotatic reflexes, with the exception of the knee-jerk, proved difficult to standardize. With the knee-jerk, however, consistent results were obtained throughout the series of animals, and for the duration of the experiments. On the side affected by the lesion the reflex was larger and longer enduring than on the normal side, and occasionally this leg retained a residue of the extension. Yet if the animal relaxed during examination the difference between the sides diminished, until on the verge of sleep the jerks became symmetrical, and both of the loose type previously characteristic of the side opposite the lesion. Clearly, the original difference between the sides was due to the operation of active flexion in checking the normal jerk and the lack of such flexion on the incompletely innervated side. Certainly the contralateral spinal-extensor centres were not depressed. The occasional tendency to retain extension after the knee-jerk might again be taken as evidence of the opposite state. But the lack of clonus in the post-operative syndrome and of a clasp-knife phenomenon, indeed the conspicuous absence of all signs of spasticity, together with the very moderate resistance opposed to passive movement, sufficiently demonstrate that

severing the pyramid had not increased the excitability of the spinal-extensor centres as does the hemiplegic lesion of man.

The failure of the extensor centres of the cord to be appreciably depressed by section of the pyramid is not surprising, for the methods of testing were crude. Indeed, the weakness and poor joint-fixation previously alluded to may be this depression in another aspect. On the other hand, the failure of the lesion to reproduce the hyper-excitability of the extensor mechanisms, which is the basis of spasticity in the hemiplegic condition of man, involves other considerations. These may more profitably be pursued after the evidence from cortical ablation and stimulation has been presented.

Having raised the question of a possible contribution of sensory disturbances to the total functional defect, the measures taken to evaluate this complication may be briefly discussed. The selection of the trapezoid body as the level of lesion was dictated by the desirability of interposing an indifferent structure between the lesion and the presumably deeper-lying ascending tracts.

To get a measure of the effect of proprioceptive lesions, the right posterior column was cut in the first cervical segment in two animals, and these were studied by the same methods as the animals with severed pyramids, one of them for a year. Pal-Weigert preparations confirmed the completeness of the latter lesion. The consequences of this operation for the placing and hopping reactions, and for posture in general, resembled in kind the effects of section of the pyramid, but were less in degree; the same general deficiency in the use of the legs appeared. With the passage of months, however, only a preferential use of the incompletely innervated extremities in placing, hopping, pawing and clawing remained to indicate the presence of a lesion. Certainly, therefore, the more lasting effects of the pyramid section may be ascribed to destruction of the descending pathway rather than to inadvertent injury to the ascending sensory systems, even one neuron higher up.

The manifold and enduring losses of function following upon section of the pyramid may then be accepted as those of a cortico-spinal lesion. Whether expressed in terms of unit reactions—placing, hopping, pawing or clawing—which were found to be deficient, or in the more general terms of loss of excitation at the final common neuron, the full extent of the defect has probably gone unappreciated. As it stands, however, certain features characterize it. First, the effect on flexor and on extensor mechanisms is unequal, in conformity with their unequal representation in the motor cortex. Secondly, phasic movements are

impaired with the preservation of the tonic or postural. These results might both have been expected. On the other hand, the absence of spasticity, and indeed of evidence of release of any lower mechanism, is a notable feature in the syndrome, upon which the results of cortical ablation and stimulation throw some light.

Secondary ablation of motor cortex.—Six months after the original operation, when the resulting symptomatology seemed stationary, one motor cortex was exposed in four of the five still surviving animals, explored electrically and excised. In two animals the cortex removed was on the side of the original lesion, and after three weeks additional survival these were killed for Marchi preparations. In the other pair, the contralateral cortex was ablated. These animals were allowed to survive for six months, when they were then killed and examined by Weigert's method. The objects of these ablations were chiefly anatomical, e.g. Marchi preparations to check the completeness of the cortico-spinal lesion, and Weigert to reveal any admixture of fibres other than cortico-spinal in the pyramid.

Study of the living animals after these secondary ablations was most suggestive. When cortical removal was superimposed on section of a pyramid, there remained, after the post-operative exacerbation of the old symptoms had passed off, a slight but definite rigidity in the affected legs as a new contribution to the syndrome. When the new lesion was contralateral to the original one, the results were greater and more complex. At first, placing and hopping were improved on the side opposite the original lesion, and abolished contralateral to the cortical lesion. Later these reactions became equally deficient on the two sides. The gait, however, was not thus rendered symmetrical, for wider circumduction still distinguished the limbs affected by the pyramid lesion. The superficial reflexes and the flexor myotatic reflexes had high thresholds on both sides, whereas the knee-jerk and the positive supporting reaction were more easily elicited and extension was longer maintained in the limbs opposite the cortical lesion. Even six months later, a lesser mobility of the extremities opposite the cortical lesion and a slightly greater resistance to passive flexion remained to indicate that the abnormality produced by the cortical lesion was in some way graver than that established by the subcortical lesion. To be sure, these experiments are few in number and the quality they deal with, namely spasticity, is a subtle one. In time the series will be extended. Yet inadequate as they are, the results of stimulation of the cortex lend them support and invest them with a significance sufficient to warrant their being put on record.

Stimulation of the motor cortex.—The motor cortex of both sides in all the cats but one was explored electrically, either previous to ablation or before the animal was killed. The extent of any previous cortical ablation was also checked by re-stimulation. The stimulating was performed under light ether anæsthesia, with a unipolar electrode delivering a 60 cycle sine wave current. The apparatus (designed by Mr. Myers) permitted determination of threshold in terms either of voltage or of current. Posture played a decisive rôle in the results. The first five animals were studied in the usual manner—back up, legs dependent. Thereafter the position was reversed and the stimulating done in that stage of ether anæsthesia which produces an extension simulating decerebrate rigidity.

From the normal cortex the usual movements of the contralateral fore and hind legs were obtained, chiefly of flexion, but as progressively lighter anæsthesia was induced, there was increasing bilateral and extensor activity. The responses in the face, eyes, tongue and jaws were initially bilateral. When the cats were in the supine posture, however, the threshold effect of cortical stimulation was not contraction, but a relaxation of any tonic or clonic extensor state present in the limbs—gravity serving to demonstrate the relaxation. From 0·25 to 0·5 volts more was commonly required to produce active flexion from the same point. In these circumstances the cortical pattern in the cat is constituted of points which are inhibitory to extension and excitatory to flexion, with the former possessing the lower threshold of activity. Extensor points are so few and unstable in the cat's cortex and a flexor tonus such a rare state, that a corresponding investigation of extensor excitation and possible flexor inhibition could not be made.

When stimulating the cortex after division of its projection path at the level of the trapezoid body, the position of the animal and the depth of anæsthesia were all important. The first five routine stimulations demonstrated the preservation of the cortical facial and trigeminal innervations. And in one animal (No. 10) the lateral border of the anterior sigmoid gyrus gave a curious slow retraction and flexion of the opposite fore-limb, and that was all. On the other hand, the last four stimulations performed with the animal lying supine and with the legs tonically extended or in clonus, gave quite another result. For now from the presumably "silenced" sigmoid gyri, relaxation of the extensor tonus or clonus was obtained, and in a pattern corresponding to the fore and hind leg patterns of the normal cortex. But on increasing the strength of the stimulation this relaxation was not followed by flexion, as in the

normal, but only by more rapid or more enduring relaxation. The relaxation or inhibition of extensor tone thus obtained was never instantaneous. The limb did not flop, but gradually over many seconds, the rate depending both on the amount of the extensor tone and on the strength of the stimulus, the extended limb relaxed, but only while the stimulation was acting. Indeed, by applying and removing the electrode, relaxation could be made to proceed in a cog-wheel fashion. Moreover, against a strong extensor tonus or clonus, inhibition might last only for the duration of the stimulation and not always even for that, the extensor centres frequently escaping. Relaxation was obtained with equal facility from the normal cortex, and at a slightly lower threshold. In cat 13, for example, relaxation of extensor tone in the hind legs on the normal side occurred at 1·75 volts, and on the side on which the pyramid was divided at 2·0 volts. But the flexion which supervened on the normal side with any increase of stimulus above threshold limited the study of inhibition there to the threshold response. Exploration of the cortex contiguous with the motor area, especially of the gyrus proreus and the entire convexity of parietal, occipital and temporal lobes, with voltage up to that producing generalized contractions, revealed no other region exercising this inhibition. The number of these successful stimulation experiments, like that of the ablation experiments, is few, but a second series of crucial experiments has already confirmed and amplified the original findings.

The evidence assembled now seems to offer an explanation of the absence of spasticity, or of "release" in any form, from the syndrome of a pyramidal lesion, and also of the differences between the effects of section of a pyramid and of cortical ablation. Apparently, excitatory and inhibitory effects of cortical activity are dissociated, in large part at least, at some prespinal level. The excitatory component is then transmitted directly to the spinal cord along the cortico-spinal tract, while the inhibitory component must be relayed through prespinal centres, finally to reach the cord along other descending pathways. The small difference in the inhibitory threshold between the normal cortex and that on the side of pyramidal section may indicate that the prespinal dissociation was less than complete. The pyramidal section, by destroying the first excitor component which is largely flexor, produced the manifold deficit described, one aspect of which was uninterrupted extension. Yet by preserving virtually intact the second inhibitory component, the syndrome was kept free of evidence of subcortical release, as rigidity and spasticity. These are the additional

contribution to the syndrome of cortical lesion when both components of cortical function are destroyed.

Previous work, notably that of Graham Brown (1913), Weed (1914), and Cobb, Bailey and Holtz (1917) has dealt with pre-spinal inhibitory mechanisms of the cortico-ponto-cerebello-rubral variety and other work, Rademaker's (1926) for instance, has shown that in cats, at least, the rubro-spinal tract serves inhibition to the cord. The augmenting influence of hemi-decerebellation on the excitability of the opposite motor cortex, first reported by Risien Russell (1894), likewise fits into the concept of a cortical inhibition exercised through the cerebellum. And certain aspects of cerebellar disease in man are in conformity with this view. Although the cortico-pontine collaterals of the pyramidal system offer a possible anatomical pathway for such inhibition, the present study has, in fact, provided no evidence to indicate either what pre-spinal course inhibition pursues, or whether systems of collaterals, or of independent neurons, or both, deliver inhibition to the presumed pre-spinal centres. If multiple systems be used, as for instance a cortico-striatal system, a cortico-rubral and a cortico-ponto-cerebello-rubral, lesions at different levels in the brain-stem might well produce different syndromes. This would seem to be the case in man. If, on the other hand, only one system is involved, the results of brain-stem lesions should be simpler. Further analysis will be required to determine how the inhibition operates. Nor is it unlikely that the complexity of the mechanism may vary in different species. The present study provides a point of departure only in the study of cortical inhibition, in the demonstration that in part at least, and that a large part, this threshold activity of the motor cortex is still exercised after destruction of the cortico-spinal pathway below its last large supra-segmental connection.

Anatomical Study.

The central nervous system alone came under anatomical scrutiny. No contracture or atrophy developed in the skeletal musculature, nor disturbance in any other organ to give indication for further exploration. Investigation of the central nervous system was organized to determine the site and extent of the descending degeneration which it was the specific aim of the original lesions to produce, and secondly, of the ascending degeneration which might be the concomitant of this. To determine the descending degeneration sections were taken at the medullary level just below the trapezoid body, and from the C_7 and L_4

spinal segments. Sections through the lesion and just above, or at the decussation of the pyramids, were sometimes examined too. In looking for ascending degeneration sections from the middle third of the pons and from other levels up to the thalamus were prepared in two animals. Standard Marchi or Pal-Weigert technique was used according to the post-operative survival time, and serial sections were cut at 15μ.

The descending degeneration (figs. 2 and 3) demonstrated the unilaterality of the lesions. With the exception of the animal in which the brain had herniated into the defect in the skull, and a tiny medial strand in one other brain, the degeneration was confined to the pyramid on the side of lesion. The lateral limit of the degeneration was also strikingly constant; only its depth varied. Just below the level of the lesion the disappearance of fibres from the pyramid was complete. More caudally, fibres and bundles of fibres appeared in the field of degeneration. These, seen best in Weigert preparations, swung in in arcs in the plane of section, obviously in the course of the strands sweeping down from the nuclei of the posterior column. In the lateral column of the spinal cord the now crossed degeneration reached the lumbar region in considerable density and throughout the cervical region scattered degenerated fibres were unmistakable in the right lateral column in the position of the pyramidal tract in cases in which the left pyramid was demonstrably intact. Descending systems other than the cortico-spinal were entirely free of degeneration.

The ascending degeneration, on the contrary, involved several systems (figs. 1 and 2). In the cortico-spinal system retrograde degeneration varied considerably from a mere scattering of blackened fibres in the pons to a fairly dense degeneration, with traces up the brachium pontis on both sides. The anticipated destruction in the lateral lemniscus was fairly equally distributed to the two sides. In the medial lemniscus the degeneration, although variable, generally exceeded expectation; it was bilateral, but much heavier on the side of lesion. And here it was traceable in diminishing density to the ventrolateral border of the thalamus (fig. 1). The small crossed degeneration in the medial lemniscus may be ascribed to the strands of internal arcuate fibres which were seen swinging through the pyramid on the side of their origin, but the massive homolateral degeneration requires a more substantial basis. After removal of the motor cortex, the corresponding pyramid was far from depleted of fibres, as may be seen by comparison of the two sides in fig. 5. Yet at the cervical level the degeneration on the two sides were approximately equal. If the surviving fibres in the

one pyramid be those contributing the ascending degeneration to the lemniscus, as seems most likely, then the pyramid, like the cortex, is a mixture of the ascending and descending systems which are the afferent and efferent pathways for the same body of reactions. And the physiological controls in the sensory component assume increased importance. Yet the constancy of the descending degeneration stands in contrast with the variability of the ascending, to indicate again that the remarkably standardized syndrome of pyramid section must depend upon the correspondingly standardized motor destruction.

More important to the argument developed in the physiological section of this paper, and based on the retention by the motor cortex of inhibitory activity while its excitor function is lost following severance of a pyramid, is the question as to whether the pyramid contains all the fibres of motor-cortical origin reaching its level. On this point secondary ablation of this cortex, six months after a pyramidal lesion of the same side, affords information. Deep to the pyramid, and extending lateral to it, is a field of fibres, chiefly the lemniscus with an admixture of fibres of cortical origin sufficient to give a new Marchi reaction. Many of these fibres are cortico-cerebellar, swinging back, even far caudally in the medulla, as Swank has described (1934). Occasional fibres were traced to the inferior olives. Still others went into the reticular formation, perhaps to cranial nerve nuclei. But none appeared to penetrate to the cord, not even in the specific instance in which stimulation of the cortex had evoked a motor reaction in the forelimb. In view of the fact that inhibition was equally effective on extensor states in the fore and hind limbs, and, after the conditions necessary for its demonstration were fully appreciated, quite constant from animal to animal, the occasional cortico-spinal fibre which may survive pyramid section, cannot be responsible for the inhibition so vigorously exercised by the cortex.

Comment.

Severing the pyramids is an experiment which has been tried repeatedly, from Starlinger's (1894-97) early attempts on dogs to Barron's (1934) recent work with rats, and Marshall's (1934), with cats. Marshall's most recent paper has reviewed this literature in detail. The more rigorous standards now adopted in assessing the degree of recovery and of residual motor defect have made necessary this repetition of a simple experiment. That the standards are still imperfect is illustrated by comparing Marshall's latest report with the present study. Further repetition of the experiment as knowledge of cortical

activity enlarges and means of testing improve, will, it is certain, demonstrate that the present observations are still imperfect.

The main contribution of the present study to an understanding of the sequels of a lesion in the voluntary motor pathway is the discovery of the pre-spinal dissociation of the inhibition and excitation of cortical origin, with the destruction of the latter function, only, by section of the pyramid. A second contribution has also been made in the demonstration that the effects of this pre-spinal lesion are in their entirety not transitory, but are probably permanent. On this, which is a fundamental point involving the plasticity of the cortex, the present study departs most widely from the observations and conclusions of previous workers. Yet even so, Marshall's (1934) recent study of the effects of lesion of the pyramid on the placing reactions foreshadowed this in the incomplete recovery found months after operation in some of his animals in certain aspects of their deficiency. The source of this discrepancy probably lies in the lesions produced, for the ten prepared for this study seem to be unique in their unilaterality and completeness. Certainly time was allowed in these for recovery beyond that permitted generally by previous investigators of such lesions.

A year, or even six months, is a relatively long period in the life of a cat, yet for such a time each element of the original syndrome with one minor exception remained demonstrable. Recovery was quantitative and unstable. Certain original difficulties, such as dragging the toes, were overcome by circumduction of the limb. On the other hand, many specific reactions were depressed and the general usage of the limb diminished for the duration of the experiments. At the level of the final neuron the crude test of the response to pin prick showed, after the first few days, no further recovery in the raised threshold of the spinal flexor mechanism. Certainly the defect was easily compensated, either by increased strength of stimulation or by raising the animal's general level of excitation. Highly organized reactions exhibited a large degree of spontaneous improvement. Yet the more carefully the fundamental defect was disentangled from the complex pattern of even the simplest action, the more stable did the syndrome appear, until ultimately in such analysis the irreparability of the physical lesion was expressed in the permanent disability of the living animal.

Summary.

The right pyramid was cut at the level of the trapezoid body in ten adult cats, and secondary ablation of motor cortex was performed in

four cases. During survival periods of from three weeks to a year the animals were observed, and at some time the motor cortex of both sides was stimulated electrically. Subsequently, specimens of brain-stem and cord were prepared by Marchi or Pal-Weigert technique for studies of degeneration.

The loss of function may be described either in terms of specific reactions such as placing and hopping, pawing and clawing which were lost or diminished; or it may be expressed as a loss of phasic activity, chiefly flexor; or again it appears as a raised threshold of the spinal flexor centres. In any form, it is permanent. The extensor mechanisms of the cord are not appreciably affected.

Secondary ablation of motor cortex adds to the syndrome of the pyramidal lesion a degree of rigidity, hitherto absent.

Stimulation of the motor cortex demonstrates the retention there of inhibitory activity, with the loss of excitation, indicating a pre-spinal dissociation, in large part at least, of these two elements of cortical function.

Anatomical studies showed descending degeneration confined to one pyramid, with a large crossed and a small uncrossed component in the lateral columns of the cord. Ascending degeneration involved the lateral lemnisci of both sides and the medial lemniscus chiefly of the side of lesion. This degeneration of the medial lemniscus is ascribed to the commingling of ascending with descending fibres in the pyramid, making this like the corresponding area in the cortex, a sensori-motor system.

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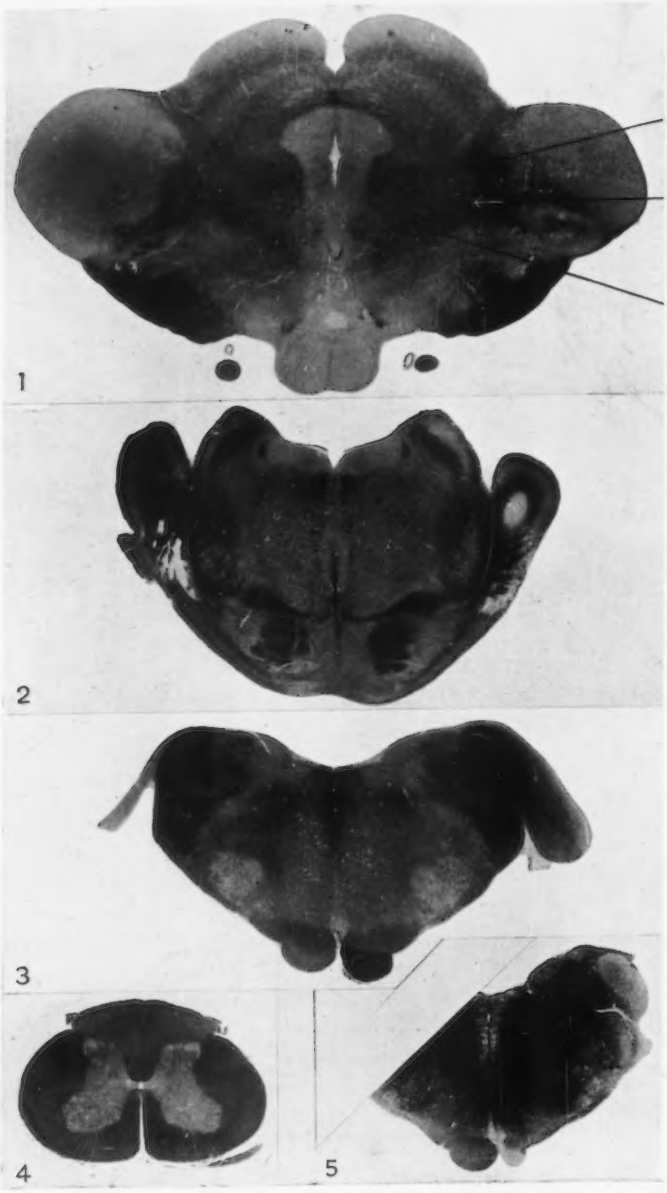
PLATE XI.



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DESCRIPTION OF PLATE.

FIGS. 1-5.—Marchi preparations showing the ascending and descending degenerations produced by a lesion of the pyramid of three weeks' standing.

FIG. 1.—Transition from midbrain to thalamus; degenerated fibres scattered throughout the ventrolateral tegmental fields where indicated by the arrows.

FIG. 2.—Middle third of pons; scattered degeneration throughout the entire lemniscus system, densest in the right medial lemniscus.

FIG. 3.—Medulla; below the trapezoid body; degeneration of the entire right pyramid.

FIG. 4.—C7; degeneration in the left corticospinal tract.

FIG. 5.—Pal-Weigert preparation of the medulla below the trapezoid body, taken six months after ablation of the left motor cortex and one year after sectioning the right pyramid, and showing the unequal effect of these lesions on the pyramids.

AN INVESTIGATION OF THE NERVOUS CONTROL OF DEFÆCATION.

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PAGE

I. INTRODUCTION 256
II. METHOD 257
III. THE EFFECTS OF LESIONS OF THE SACRAL ROOTS 259
IV. TRANSVERSE LESIONS RESULTING IN REFLEXLY ACTIVE STATES 269
V. THE NORMAL RECTUM AND ANAL SPHINCTER 279
VI. THE PERIPHERAL AUTONOMY OF DEFÆCATION FOLLOWING DESTRUCTION OF SACRAL INNERVATION 282
VII. THE REGULATION OF DEFÆCATION BY THE CENTRAL NERVOUS SYSTEM .. 288
The Postural Tone of the Sphincter Ani and Rectum 289
Spinal Reflex Activity 292
The Sympathetic Nervous Pathway and the Participation of the Pelvic Colon 300
VIII. SUMMARY OF CONCLUSIONS 305

I.—INTRODUCTION.

THE investigations of Hurst [19] have established that inefficiency in defæcation commonly results from nervous diseases and is accompanied by fæcal accumulation in the rectum (dyschezia). The delivery of fæcal material to the rectum in these cases is not functionally impaired. To the lack of sensation of desire for defæcation and consequent absence of voluntary effort, Hurst attributes the greater part of the disturbance. Appropriate voluntary effort does not suffice to correct the defect. The mechanism by which the sphincter ani is normally induced to relax is not clear, and is commonly attributed to spinal reflex activity of some kind, possibly stimulated by movement within the colon [11], assisted by willed straining. The diminished tone of the anal sphincter consequent to lesions of the sacral innervation gives reason for the prevalent view that a spinal "centre" for defæcation lies within the sacral segments, and that complete fæcal incontinence in this type of nervous lesion results from loss of the sphincteric mechanism. Even in complete transverse lesions of the cauda equina, however, defæcation has been observed to occur periodically with appropriate

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further relaxation of the sphincter ("automatic defæcation" Müller [27]. and Bálint and Benedict [3]). It is not known whether this is identical with the similar phenomenon observed following transverse lesions of the spinal cord and then associated with evidence of rectal contractility (Head and Riddoch [17].) The precise nature of the reflex activity of the sacral segments in relation to defæcation and to the clinical tone of the sphincter ani is therefore confused and ill-defined.

In the present study we have attempted to define the activity of the rectum and anal sphincter in "automatic defæcation," and to analyse the nervous control of the evacuating mechanism in conditions where spinal reflex activity is present, and in the normal subject.

II.—Method.

In each experiment a rubber balloon, which can contain 50 c.c. of air before stretching of the rubber commences, was introduced within the rectum by digital manipulation so that its nearest portion lay over 10 cm. from the anus. Its base was attached by rubber solution to a gum-elastic catheter of 4 mm. outside diameter, sufficiently rigid to prevent its curling within the rectum in the first 10 to 20 cm., and this junction of balloon and catheter was made with the wider distal end of the latter so that occlusion by kinking was less liable to occur (fig. 1B, *d*). This rectal balloon was moderately distended (30 c.c.) to allow its complete unfolding before the experiment commenced. The catheter was attached at its outer end to thick rubber pressure tubing leading to a manometer. A second similar catheter with open end bound to the region of the neck of the balloon (fig. 1B, *e*) is arranged so that fluid may be run from a graduated reservoir into the space between the rectal balloon and the sphincter (fig. 1B, *f*). This space, for convenience of description, we term the "intervening segment." A small glass chamber with fluid level, of the kind used for recording vesical pressures (7), communicated the pressure of this fluid with the air in a second manometric system.

Having experimented with a variety of small balloons attached in various ways to the region of the catheters related to the anal sphincter, we found most satisfactory a balloon mounted on a small brass obturator (fig. 1A, at *a* and B at *g*) in such a way that the upper surface was solid and did not transmit rectal pressure. It was sufficiently rigid to ensure the apposition of the distensible rubber wall to the anal canal with slight bulge above or below when distended, and with narrow (6 mm.) stem to allow the sphincter to close as much as possible when

the air space was not distended. The pressure of air within the sphincteric recorder was registered by means of its attachment to thick pressure tubing (fig. 1A, *b*) leading to a third manometer.

The amount of distension of the rectal and sphincteric recording systems was regulated by the introduction of specified amounts of air within the system by means of a syringe. The pressures registered for particular quantities of air injected form the data from which graphs comparing different nervous states are derived. We were aware that the use of air as a medium for pressure registration means that the volumes of air are not absolute, owing to the smaller volume at greater

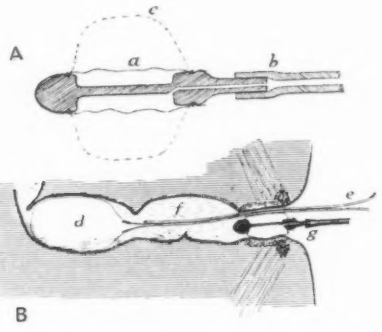


FIG. 1.—Diagrammatic representation of the method of recording used. The sectional diagram A shows the construction of the recorder of pressures in the sphincter ani. A brass core with solid head has a thin rubber membrane *a* attached so that it may be distended by pressure applied through the tubing *b*. The diagrammatic section B shows the rectal balloon *d*, in place, with the additional catheter *e* attached to its neck and communicating with the space *f* ("intervening segment"). The recorder of sphincteric pressure is shown in place at *g*.

pressures. The volume therefore does not increase in the linear fashion in which the results are graphed. The use of water media and indistensible membranes would be more ideal for volumetric estimations but has disadvantages in the rapid introduction of additional increments of distension. The factors involved in any mathematical representation of the tension at the circumference of an object of increasing circular diameter are of such complexity that we have relied upon the above more simple method, designed only to give some graphic representation to phenomena which can readily be observed and controlled by clinical examination.

Apart from some early experiments the patient lay upon his left side, but we found no distinct difference between the records in this posture

and those with the same patient supine. The movements of the abdomen were recorded by balloon applied to the epigastrium beneath a binder.

The manometers used were of glass with thick rubber diaphragm, as used in our earlier work on the bladder [7], and the movements of the membrane recorded photographically by reflected beam of light.

The human rectum is usually stated by anatomists to be 12 to 15 cm. in length, and terminates in the anal canal which is some 2·5 to 3·5 cm. in length. Dr. Hurst informs us that in sigmoidoscopic examination of the living the pelvi-rectal junction lies almost constantly only 11·3 cm. (4½ in.) from the outer extremity of the anal canal. The recorder we have used for the sphincter ani (fig. 1, A) in almost all experiments (where others were used in early experiments, this is mentioned in the text) has an inflatable portion 2·5 cm. in length. Its diameter when inflated until the rubber commences to stretch is 4 cm. Digital examination of the anal canal in cases of cauda equina lesion reveals that the whole canal has sphincteric function, and, as will be related in the text, slow contraction may be observed in the surrounding perineum. The rectal balloon was placed well beyond the sphincteric recorder, and often moved higher during the experiment. Owing to the varying diameter of the rectum we have made no attempt to occlude the passage with the rectal balloon, and fluid run into the intervening segment often ran beyond it in considerable quantities. This rectal balloon, when distended until the rubber just began to stretch, was 4·5 cm. in diameter and 5·5 cm. in length. Distension to greater volumes was not attempted as the less ordinarily suffice to excite contraction of the organ. Distension of a balloon within the lumen of the rectum or anal sphincter acts as a stimulus for a local contraction. It may be objected that the local disturbance excited by the presence of the recorder itself serves to modify the response to other changes. As the relaxations of the sphincter here recorded also could be watched by the observer when the only foreign body within the sphincter was the narrow gum-elastic catheter going to the rectal balloon, we feel certain that in this case this objection cannot hold.

III.—The Effects of Lesions of the Sacral Roots.

It is convenient to consider in each investigation, first the state of the rectum and sphincter, and secondly the relationship obtaining between the two.

Case 1.—H. F., male, aged 46, under the care of the late Dr. Collier. Compression of cauda equina by neurofibroma.

Frequency and urgency of micturition for three years. For two years inability to control bowel evacuation after taking laxatives. Involuntary micturition for two years, readily provoked by coughing and straining for six months. No power of delaying discharge or of interrupting the stream. Bowels very constipated for three months. He stated that he could digitally feel fæces in his rectum, but lacked the power to expel. After taking laxatives evacuation occurred without his knowledge or control. After purgatives this phenomenon was preceded by a sensation of pain in the lower abdomen. Tends to micturate if strains. Twelve months before admission persistent pain over dorsum of foot for two months, and followed by weakness of the left ankle. On examination he showed wasting and weakness of glutei, calf and pretibial muscles, and intrinsic muscles of feet, greater left than right. Marked bulging of perineum on coughing or straining. Knee-jerks very active, right ankle-jerk present, left absent. Abdominal reflexes present. Plantar responses flexor. Anal reflex absent, sphincter relaxed, but not patulous. Deep, but not quite complete loss of sensation to cotton-wool, pin-point and heat and cold over S 3, 4 and 5. Slight loss over S 2. Complete subarachnoid block with Froin's syndrome. Surgical removal of elongated neurofibroma lying among the roots of the cauda equina in the midline and appearing to arise from the filum terminale.

Distension of the rectal balloon in this patient by the sudden introduction of volumes of air up to 50 c.c. evoked evidence of active contractile response. The first 5 c.c. injected brought about a rise of pressure of 23 cm. water, with well-maintained subsequent level (fig. 26, Plate XIV, at *b*). A second 5 c.c. evoked not only a smaller further rise to 27·5 cm. pressure, but a delayed wave of increased pressure (fig. 26, *d*, *e*) which subsided to leave a maintained level of 20 cm. pressure. A further increment of 10 c.c. air added to the balloon now evoked an immediate rise to a peak of 45 cm. water pressure (fig. 26 at *g*) followed by a larger delayed wave of increased pressure, with eventual subsidence to a fresh level of 28 cm. pressure (fig. 26 at *g*, *h*) followed by a series of fluctuations of approximately fifteen seconds' duration. This delayed wave of pressure induced by sudden distension was found to be regularly elicited by sudden distension, and may be likened to the similar "secondary" wave of pressure obtainable from the bladder by sudden stretch of the vesical wall (8).

Distension of the air space of the sphincteric recorder gave rise to a sudden rise of pressure which subsides slowly. When the distension was made in small increments, 1 c.c. at a time at eight seconds' intervals, and the resulting pressures charted in a graph (shown in fig. 12, Plate XII), it will be seen that following the sharp peak of each initial rise of pressure the fall is steeper as the sphincter is further distended. At

5 c.c. (30 c.c. being required to distend the recorder fully to a diameter of 4 cm.), this adaptation of pressure to increased volume is found to vary, being at times rapid, at times non-existent. At this degree of distension of the sphincter slow rounded fluctuations of about ninety seconds' interval were found to be occurring in the state of the sphincter at any constant volume (fig. 27, Plate XIV). The further the sphincter was distended the more obvious these fluctuations became. The adaptation of the sphincter to a suddenly imposed increase of volume of contents appeared steeper when related to the crest of one of the spontaneous fluctuations than when related to the trough. If distension to such a degree were made suddenly by the injection of a single large amount of air into the recorder the pressure rises steeply to a sharp peak and immediately falls to a trough, followed by a reassertion of tone at a slightly higher level (fig. 26 at *a*). This primary relaxation and later reassertion of tone appears identical with the curve published by Gowers [16] of the resistance given to the sudden insertion of an object within the lumen of the sphincter. A momentary increase of abdominal pressure brought about passively by the observer elicits in most striking way a similar relaxation of the sphincter (fig. 27, at *a*). The relaxation here has, however, a delay in onset of over three seconds.

Diminution of the content of the recorder in the sphincter resulted in immediate parallel fall in pressure, but if the lower volume were now kept constant the pressure gradually rose, so that the sphincter maintained an increased grip on the recorder. Movement of the recorder within the sphincter excited no change apart from the fall of pressure when the recorder passed within the rectum or out beyond the sphincter.

Manipulations of the recorder within the sphincter or in volume of the recorder had not the slightest effect on the rectal pressure when that was recorded concurrently. On the other hand, the sphincter was found to be influenced in the most remarkable degree by changes within the rectum. If, the sphincter ani being moderately distended, the rectal balloon were suddenly inflated there ensued a deep relaxation of the pressure exerted by the sphincter ani (fig. 26, Plate XIV, at *c*, *f* and *i*). The relaxation outlasted in duration the induced wave of rectal contraction (fig. 26 at *i*) when that was present, and still occurred when no such wave occurs (fig. 26 at *c*). There is a delay in its onset which suggests that its appearance is related to the onset of the induced rectal contraction wave. A further distension during the trough of this relaxation excited further relaxation, revealing a capacity of the effect to summate.

If fluid were run into the segment of rectum intervening between the rectal balloon and the sphincter recorder ("intervening segment," fig. 1B, *f*) there ensued a rise of rectal pressure of wave form accompanied by a very deep relaxation of the sphincter (fig. 26, Plate XIV, *m*, *n* and fig. 2 at *c*). The slowly developing rise of contraction upon the rectal balloon is clearly not related to any direct mechanical pressure of fluid against the rectal balloon, which was here some 15 cm. within the anus, and is a stimulated contraction in the rectal wall applied to the balloon. The pressure in the fluid in the intervening segment reveals that a more brief and perhaps earlier contraction had occurred in this region of the rectum, and was followed by a further small contraction, *o*, fig. 26, not revealed in the pressure of the higher segment. The same series of events is shown in fig. 2, when the intervening segment is distended by 20 c.c. fluid between *a* and *b*, with resulting wave of rectal pressure at *c* and relaxation of the sphincter ani at *d*. Here the pressure in the intervening segment when the inflow is shut off at *b* reveals a declining wave of pressure. We imagine that the introduction of a small quantity of fluid in this manner subjects a greater area of the rectum to stretch, and thus provokes a greater rectal contraction than does distension of the rectal balloon. Injection of a small quantity of fluid evokes a contraction only of the intervening segment. The mechanism of relaxation of the sphincter in each case appears identical and is related to tension on the wall of the rectum.

As mentioned earlier, the pressure within the sphincter ani underwent long slow fluctuations, and when the rectum was distended there occurred with some of these one or more rectal contractions as at *j*, fig. 26. Such contractions showed a relationship with the relaxation of the sphincter which suggested an opposite, or reciprocal, correspondence between the two, so that spontaneous active contractions of the rectum are accompanied by some corresponding relaxation of the sphincter. This relationship does not hold in inverse manner, for often no rectal contraction accompanies the long slow spontaneous fluctuations in the sphincter (fig. 26, at *p*). The clean-cut relaxation of the sphincter in response to rectal distension is by contrast a transitory phenomenon induced by the phase of increasing tension on the rectal muscle. The period of evacuation will be observed to begin when greatest increase of rectal pressure coincides with greatest relaxation of the sphincter, and declines only as the sphincter closes (fig. 2).

If fluid were run continuously into the intervening segment over a long interval the induced disturbance in the rectum took the form of a

series of waves of contraction growing less frequent when the flow is stopped (fig. 2, *e*, *f*, *g*). The sphincter ani relaxed rapidly and maintained a relaxed posture during the whole period of inflow. Fluctuations in this relaxation revealed an intensification of relaxation corresponding to the later half of each rectal wave. This delay in the effect of each rectal wave on the sphincter might be due to an interval of propagation of a wave of contraction downwards from balloon to sphincter, but the pressure in the intervening segment indicates that each wave of contraction tends to involve the whole rectum concurrently (fig. 2, *g*). Evidence of peristaltic contraction in this phenomenon was lacking except for the occasional occurrence of late small waves in the

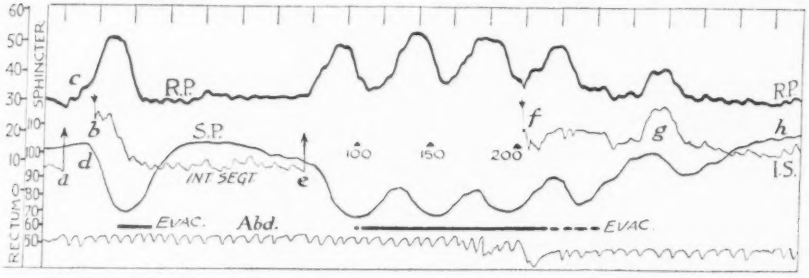


FIG. 2.—To show the effect of distension of the rectum with fluid in Case 1. The tracings in this and all subsequent figures read from left to right. The pressure within the rectal balloon is recorded by the thick line R.P., and the tension in centimetres of water is shown in the first scale. The pressure within the recorder in the sphincter ani is shown in the tracing S.P. The movements of the abdominal wall in the region of the umbilicus is shown in the tracing Abd, where a downward movement represents inspiration. The pressure in the catheter connecting the reservoir with the intervening segment is shown as the thin line INT. SEGT. At *a* 20 c.c. of warm normal saline is allowed to flow from the reservoir into the intervening segment and at *b* the tap to the reservoir is closed. It is again opened from *e* to *f* and 200 c.c run in. Fluid was evacuated past the sphincteric recorder in the intervals indicated by the horizontal black lines (EVAC). Time shown in vertical strokes at 10 second intervals.

intervening segment as at *o* in fig. 26. That the lack of partition between rectal balloon and intervening segment is not responsible is seen in the independence of the two curves, and is due to the low pressure of the fluid (10 to 20 cm. water pressure).

The co-ordinated contractions of the rectum and relaxation of the sphincter ani in response to progressive distension of the rectum secured evacuation of fluid past the sphincter as shown in fig. 2. The relationship of this evacuation to the phenomenon of reciprocal contraction indicates that it forms the basis of the automatic defæcation observed in this patient.

At the time of our examination automatic micturition was well established.

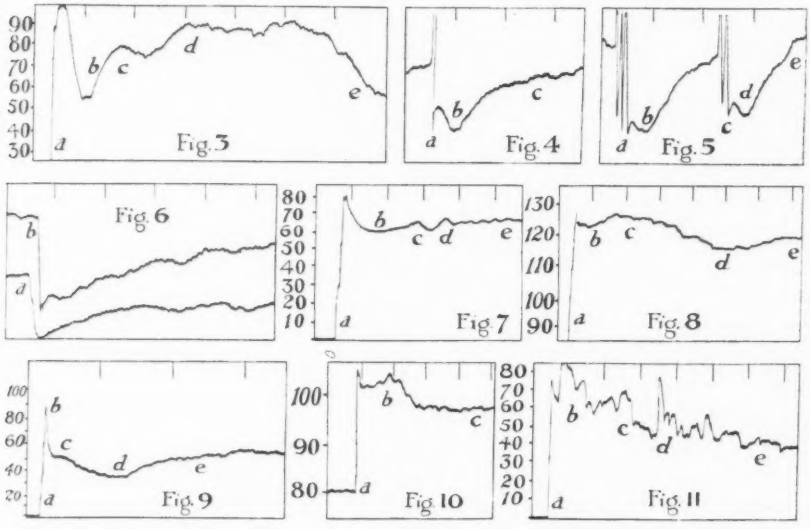
Case 2.—C. R., male, aged 25, under the care of the late Dr. Collier. Spinal arachnoiditis, involving the cauda equina.

Weakness of right foot and leg, with wasting of right leg, for five years. For eighteen months incontinence of urine occurred with exertion. He had to strain to empty his bladder voluntarily. Two years earlier for a period of twelve months he suffered from diarrhœa. Since then evacuation, which he can postpone, has occurred once or twice a day, sometimes easily, usually commenced by straining. On examination he showed slight bulging of lower abdominal muscles on straining. Gross wasting and weakness of glutei, hamstring, calves and intrinsic muscles of feet. Knee-jerks present, ankle-jerks absent. Left lower abdominal absent, others present. Plantar responses absent. Anal reflexes absent. Sphincter patulous. Slight diminution to cotton-wool, pin-point and heat and cold over sacral segments, less over lumbar segments as high as L 2. Partial subarachnoid cerebrospinal fluid block. Laminectomy D 10 to L 3 disclosed thickening of arachnoid, with cystic loculation increasing caudally. Histologically a fragment of arachnoid removed showed only fibrous tissue.

In this patient distension of the rectal balloon, as in Case 1, encountered an immediate resistance (figs. 29, 30) followed by a marked induced "secondary" wave of increased pressure, and succeeded by a moderate degree of plastic adaptation. The secondary wave of pressure was found to be more obvious when the balloon lay some 5 to 10 cm. above the sphincter ani (fig. 30 *g*) than when it lay over 10 cm. above the latter (fig. 30 *a*). This difference is largely one of threshold of stimulus, and even when the balloon was known to be at a high level secondary waves were often obtained by sudden full distension. Spontaneous fluctuations in rectal pressure were not observed.

Distension of the sphincter ani gave rise to an immediate resistance which rapidly melted when further distension ceased, and this fall of pressure was succeeded by a series of small waves of pressure at ten to fifteen seconds' intervals (fig. 3). Distension of the sphincter 1 c.c. at a time revealed low resistance with a high degree of plasticity, as seen in the resulting graph (fig. 13, Plate XII, *a*), and agreeing with its soft patulous feel in digital examination. If the sphincter were examined by gradual distension in this manner its resistance was found to vary not only in brief phases corresponding to its rapid distension or distension of the rectum, but in lasting states of greater relaxation one of which corresponded with distension of the bladder, and another with the appearance of fæcal

matter in the upper rectum. The data for the graph recorded in fig. 13*a*, were obtained at a time when reduction in volume of the sphincteric recorder from 20 to 10 c.c. was followed by an immediate drop in



FIGS. 3-11.—To illustrate the effect of sudden moderate distension of the sphincter ani. Time is shown at the top of each record in vertical strokes at 10 second intervals.

FIG. 3.—From Case 2, to show the effect of the injection of 20 c.c. of air into the sphincter recorder at *a*. The period of injection occupies a little over two seconds. The remainder of the curve shows the reactionary pressure.

FIG. 4.—Also from Case 2. 10 c.c. of air has been injected into the sphincter recorder and a stationary pressure reached. At *a* a further 10 c.c. of air is injected and immediately withdrawn within two seconds. Tensions as in scale of fig. 3.

FIG. 5.—As fig. 4, except that at *a* the manœuvre is repeated three times, and at *c* twice in rapid succession.

FIG. 6.—Also Case 2. At *a* the air within the sphincter recorder, already containing 20 c.c., is reduced to 10 c.c. Later in the experiment, following micturition, the same procedure is repeated and the resulting pressures are shown at *b*. Tensions as fig. 3.

FIG. 7.—From Case 3. At *a* 20 c.c. of air are injected into the previously empty recorder.

FIG. 8.—From Case 9. At *a* 7 c.c. of air were injected into the empty recorder.

FIG. 9.—From Case 5. At *a* 10 c.c. of air were injected into the empty recorder.

FIG. 10.—From a normal subject. At *a* an increment of about 2 c.c. was added to a recorder content of 10 c.c.

FIG. 11.—From a normal subject. The recorder was arranged so that the distensible portion was half extruding from the sphincter. At *a* 10 c.c. of air are introduced suddenly into the recorder.

pressure with gradual reassertion of a low tonic level after an interval of thirty seconds (fig. 6, *a*). A few minutes later micturition occurred, and the sphincter was then found to be more resistant. Distension by

increments of 1 c.c. now gave data for the graph fig. 13, *b*, and reduction of volume from 20 to 10 c.c. was followed by less reduction of pressure and slow recovery of much higher tone in the ensuing forty seconds (fig. 6, *b*).

The immediate trough of relaxation following a sudden moderate distension of the sphincter in this patient was so well developed (fig. 3 at *b*) that it was examined in further detail. It is not present with small increases in volume, so that the usual interval of eight seconds between observations on distension by small increments allowed sufficient time for a maintained level of pressure to be reached under these circumstances. A transitory small distension, bringing the volume back to the previous level within two seconds, did not reveal any change in existing tone. A brief distension with 10 c.c. of air was followed, however, by a lowering of the existing state of tone, reaching a trough five seconds later, and regaining the previous level in the following twenty to thirty seconds (fig. 4). A momentary stretch of the sphincter therefore induces in it a passing relaxation, and two stretches induce a less deep relaxation than three (fig. 5). The first fall in pressure following upon a sudden and *maintained* stretch is therefore a true relaxation of the sphincture.

Inflation of the rectal balloon brought about relaxation of the tone of the sphincter, as in Case 1, and the relaxation was found to be deeper, but with about the same latency, when the rectal balloon lay within 5 to 7·5 cm. of the sphincter, than when it lay 10 cm. or more above it (fig. 30, *a* and *f*). The presence or absence of a secondary wave of rectal contraction did not modify this reaction. Deflation of the rectal balloon after varying periods of inflation, brought about no change in the sphincter, but movement of the deflated rectal balloon downwards when this could be done without direct disturbance of the sphincter, excited some moderate relaxation of the sphincter (fig. 30, *d*). The effect of momentary brief distension of the rectal balloon revealed that a certain intensity of stimulation was required to effect any relaxation of the sphincter. Single brief distensions were without effect and repeated distension was necessary (fig. 29, *i*, *j*, *k*, *l*, *m*).

Progressive distension of the segment intervening between rectal balloon and sphincter brought about only slight rise of rectal pressure, but was not continued to any large volume. The sphincter in this patient showed when highly tonic the long slow fluctuations also seen in Case 1 (figs. 29, 30), and the effect of moderate progressive distension only lowered the general height of tone, with the appearance of small

fluctuations (fig. 28, *g*). There was no voluntary power over the sphincter, and no cutaneous stimulus appeared to affect it. Movement of the sphincteric recorder did not succeed in provoking any effect other than the rise or fall in pressure consistent with its passage into or out of the region of maintained tonic effect and the brief relaxation if the sphincter were thus rapidly distended. Distension of the sphincter, or movement within it, had no effect on the pressure within the rectal balloon.

Accompanying each relaxation of the sphincter induced by rectal distension in this patient not only could the slackening of the skin of the anus be directly observed but also a slow outward movement of the skin of the whole peri-anal region of the perineum. The signalling of the intensity of this relaxation revealed its exact correspondence with the relaxation of the sphincter (fig. 30 at *a*).

This patient had developed only a low grade of automatic micturition, so that small vesical contractions secured enough relaxation of the vesical sphincter to allow evacuation with straining. There was no evidence of function of the external vesical sphincter.

Case 3.—M. R., aged 30, under the care of the late Dr. Collier. Tumour causing compression of cauda equina.

History of severe pain shooting from right buttock, down back of thigh and front of leg to the toes for twenty months; nine months later difficulty in initiating micturition, replaced after three days by precipitant evacuation and incontinence. Desire to pass urine almost continuous, and urethral sensation intact. He experienced desire for defæcation but "did not seem to be able to get it away." After purgation he had difficulty in controlling defæcation. A month later his knees, ankles and feet became weak, and numbness commenced in buttocks, penis and scrotum, backs of calves and feet. On examination he showed slight weakness of flexors of right hip and knee. Knee and ankle jerks present. Abdominal reflexes present. Plantar responses indefinite but tendency to flexion. Anal reflexes absent. Loss of sensation to cotton-wool, pin-point, and heat and cold over sacral skin segments. Almost complete subarachnoid block. The cerebrospinal fluid showed Froin's syndrome. Operative removal of hæmangio-endothelioma from roots of cauda equina.

The reaction of the rectum to sudden moderate increase in the volume of the rectal balloon in this patient was an initial sharp peak of pressure followed by slow and slight adaptation (fig. 31). No induced secondary wave of pressure occurred, unless a very large volume (over 50 c.c.) of increase was made and it was then small. A small secondary wave could be induced by brief pressure on the abdominal wall or by a cough.

Distension of the sphincter ani gave a low pressure curve (fig. 14) with well-marked plastic reaction, and a single moderate distension was followed by a slight following relaxation with recovery (fig. 7, *b*, *c*, *d*) in small rhythmical waves. Movement of the recorder in the sphincter induced a similar following relaxation with recovery.

The effect of distension of the rectal balloon on the sphincter was a definite though not very deep relaxation (fig. 31). More momentary distension of the rectum such as a cough, with associated secondary wave of pressure in the rectum, was also accompanied by a relaxation of the sphincter. The rectal balloon was very low in the rectum, but further insertion of it brought no increase in reaction.

Filling the segment between balloon and sphincter with a small amount of fluid induced a moderate and progressive relaxation of the sphincter with no increase of pressure on the rectal balloon and the intervening segment (fig. 32). Progressive filling of the intervening segment with fluid induced a slow rise of rectal pressure surmounted by a series of irregular small waves, and accompanied by further relaxations of the sphincter, some of which are reciprocal to rectal waves, and each of these with slight delay in onset after the corresponding rectal wave (fig. 33).

This patient showed a contraction of the rectum with each micturition, a phenomenon we had before only observed in reflexly active spinal states [8], and not present in our other cases of cauda equina lesion. Single waves of rectal contraction accompanied spontaneous micturition when the rectum was distended, and relaxation of the sphincter ani was co-ordinated with the rectal contraction (fig. 34). The recovery of tone in the sphincter ani to a supernormal level is here more evident than in other cases, a reflection of the effect of evacuation of fluid both from the bladder and from the intervening segment. Distension of the sphincter or movement within it had no effect of the pressure recorded by the rectal balloon. Distension of the rectum gave rise to a "forcing feeling" vaguely felt in the abdomen, but to no sensation related to the pelvic region. This patient had developed an unusually powerful automatic micturition. There was no evidence of function in the external vesical sphincter.

Case 4.—F. T., aged 28, under the care of Dr. Carmichael. Compression fracture with posterior dislocation of the 11th thoracic vertebra and complete destruction of the spinal cord below the 1st lumbar segment.

Eight months earlier the patient's spine was bent acutely backwards in an accident. There was immediate loss of sensation and power of his legs.

Retention of urine necessitated catheterization: of fæces, enemata. Seven weeks later periodic incontinence of urine and fæces commenced. He presented complete flaccid paraplegia with gross wasting and absent deep reflexes. Abdominal reflexes absent below the 11th dorsal segment. Plantar responses absent. Very slight contraction of the anus could be elicited by a scratch near it. Intermittent spontaneous defæcation when stools were soft. Sphincter usually very patulous. Partial anæsthesia below D 11, complete below L 1. No sensation associated with micturition and defæcation. Sloughing sacral bedsore and perineal fistula. On admission to this hospital he was in a condition of extreme toxæmia from which he succumbed after four weeks. Autopsy revealed complete destruction of all the lumbar and 1st, 2nd, 3rd and 4th sacral segments of the spinal cord. A small piece of intact 5th sacral segment accounted for the anal reflex.

Our observations on this patient were made at the bedside, as his condition did not allow removal to the laboratory. The reaction of the rectum and sphincter to distension was recorded by mercury manometer and the results charted in terms of water pressure for comparison with Cases 1, 2 and 3. The sphincter showed a moderately plastic curve of resistance to distension (fig. 15, *a*), and at the time of examination the sphincter was less patulous than usual. The rectum had maintained a resistance to distension comparable to Cases 1, 2 and 3, but induced waves of rectal pressure were not observed (only slight distension was used). Distension of the rectum was followed by well-defined relaxation of the sphincter ani. Movement within the sphincter evoked no sudden contraction of it. There were slow long fluctuations in the tonic pressure of the sphincter. Some low degree of automaticity of micturition was present but was not closely investigated.

IV.—Transverse Lesions Resulting in Reflexly Active States.

Case 5.—G. R., male, aged 24, under the care of Dr. Carmichael. Fracture dislocation of spine with evidence of destruction of 4th thoracic segment.

Since a motor-cycle accident five months earlier he had been unable to move or feel his lower limbs. There was at first complete retention of urine and fæces. The time of first appearance of active defæcation was not noted. For eight weeks the bladder was emptied by an indwelling catheter. After two and a half months reflex flexion was first observed in the lower limbs, and after a further two weeks active incontinence of urine was observed and the catheterization discontinued. Urine evacuated involuntarily and without his knowledge every ten to fifteen minutes. The intervals had increased and he felt a peculiar feeling in the hypogastrium before evacuation commenced. No power of initiating micturition or defæcation, the latter occurred intermit-

tently without his knowledge or control only after enemata or aperients. On examination he presented complete paralysis of the intercostal muscles below the 4th, and muscles of abdomen and lower limbs. The lower limbs lay in extension, flaccid and wasted. Knee-jerks and right ankle-jerk present, left not elicited. Abdominal reflexes absent, plantar responses extensor with flexor withdrawal of the whole limb. Anal reflexes present. Rectum very distended with soft fæces. There were persistent penile erections. No ejaculation. All forms of sensation lost below the 4th thoracic segment. There was complete cerebrospinal fluid block. X-ray showed fracture of 4th, 5th and 6th thoracic vertebræ, with collapse of 5th thoracic vertebra.

Distension of the rectal balloon in this patient induced a small wave of secondary contraction followed by plastic adaptation to a new tonic level (fig. 35, Plate XV). Even distension to 50 cc. capacity excited but slight rectal secondary contraction. The sphincter ani was moderately resistant to gradual inflation (fig. 16), showing plastic adaptation at an intermediate level. Sudden moderate inflation of it met a high resistance followed by an immediate slight contraction, which was succeeded by a trough of relaxation before steady tonic contraction was reached (fig. 9), and induced a small wave of rectal contraction. Sudden inflation of the rectal balloon induced a relaxation of the sphincter with the usual duration of about twenty seconds (fig. 35). The record of sphincteric contraction showed at times an irregular jerkiness which was due to a very slight irregular contraction of the voluntary musculature of the perineum which was palpable in the region of the external sphincter. A stimulus to the sole of the foot elicited a rapid rise of all pressures with contraction of the levator ani (fig. 37), and when the rectum had been distended this resulted in a late rise of rectal pressure and subsequent evacuation (fig. 37, *b*, *d*).

Distension of the intervening segment resulted in but slight and passive rise of rectal pressure, while the sphincter relaxed moderately and irregularly (fig. 36). For evacuation to occur some additional sudden increase of pressure, such as a passive pressure on the abdominal wall, appeared to be necessary, when the train of events are similar to the effect of stimulation of the sole of the foot. Sudden distension of the sphincter or movement within it was also a stimulus for such evacuation, and both these manœuvres excited an immediate contraction of the sphincter (fig. 38). The rise of pressure in the sphincteric recorder during evacuation at *d* in fig. 37 and *b* in fig. 38 is due to the impaction of passing semi-solid fæcal material against the rubber of the recorder. It will be observed that the waves of pressure in the intervening segment are identical in time with those in the rectum. Owing to the fæcal mass

which continuously filled the rectum it was not possible to separate the rectal balloon and sphincter recorder widely.

Digital palpation of the anal sphincter encouraged a moderate tonic resistance, and a brief initial resistance to introduction of the finger was felt to be distinctly related to the outer part of the sphincter. No tonic contraction could be felt in this area. The brief contraction in response to stimulating the sole of the foot occurred in the same part of the sphincter (external sphincter). On continued palpation the sphincter became much softer and evacuation often occurred. Well developed and powerful automatic micturition was present.

Case 6.—H. M., male, aged 24, under the care of Dr. Carmichael. Fracture-dislocation of 1st lumbar vertebra with compression of spinal cord which isolated portions of the sacral segments.

Immediately after a motor-car accident six months earlier he was unable to move either leg, and the left leg felt numb. Sensation and the power of the left leg have remained unaltered, the power of the right leg gradually improved. Spasmodic involuntary flexion of the right knee and adduction at the hip during previous three months. Retention of urine necessitating catheterization for the first six weeks, then frequent involuntary evacuation over which he had no control. For some thirty seconds before micturition occurred he had a feeling of "knotting" in the lower abdomen. No bowel action for six days after the accident. Since then laxatives have secured evacuation following a warning dull ache in the lower abdomen. Constriction of the penis and straining were habitually used to assist defæcation. On examination he showed wasting of the muscles of both lower limbs. Left lower limb completely powerless. No movement at right ankle. Flexion of right knee very weak, extension fair. Extension and abduction and rotation of right thigh almost powerless, flexion and adduction of fair power. Legs lie flaccid and extended. Knee-jerks and ankle-jerks absent. Nocuous stimulation of any part of the skin area of the right sacral segments elicited plantar flexion of toes of both feet, excepting the great toe, in which there was no movement. With this reflex occurred a contraction of the whole perineum, including a faint contraction of the external anal sphincter, more brisk on the left side. Penile erection readily elicited. All forms of sensation lost below the 1st lumbar segment on the left side and the 4th lumbar segment on the right. X-ray revealed fracture dislocation of 1st lumbar vertebra.

Distension of the rectal balloon encountered a slight initial resistance followed by a slow small wave of pressure with slight final adaptation to a well-maintained tonic pressure (fig. 39). The sphincter ani was very resistant to the initial stages of gradual inflation (fig. 17, *a*), but as inflation proceeded the resistance fell, so that the sphincter became very soft and patulous. Evacuation did not at this time occur, but both earlier

and immediately subsequent inflation of the sphincter elicited evacuation, and the later fall in the curve is attributed to stimulation of rectal contraction. When a sudden inflation of the sphincter was made the initial high resistance often passed into a very steep fall in pressure in the sphincter in which some jerky contraction heralded a rise of rectal pressure and a large evacuation. At the end of the investigation, when further evacuations of a large quantity of fæcal matter had been induced by other stimuli, the sphincter ani was found to be much more resistant to gradual distension, and the graph of resistance to gradual filling now showed a very steep rise indeed so that the limit of our pressure registration was soon reached (fig. 17, *b*). In view of the large quantity of fæcal material evacuated this heightening of tone of the sphincter may be related to lessening of distension of the pelvic colon as well as of the upper rectum.

Inflation of the rectal balloon brought about a moderate relaxation of the sphincter (fig. 39). Greater inflation of the rectal balloon was followed by deeper and more prolonged relaxation of the sphincter ani. Slight jerky contractions of the external sphincter continued throughout the trough of these relaxations, and do not appear to be affected. On account of loading of the rectum with fæcal matter it was not practicable to investigate the effect of distension of the intervening segment. Spontaneous evacuation was, however, observed, and was preceded by a slow lowering of the tension of the sphincter during which the pressure within the rectum rose only very slightly in the first thirty seconds and mounted gradually into a large wave of high pressure with such force of evacuation of solid fæces as to bring about a rise of pressure in the sphincter recorder. On another occasion a rhythmical series of small waves surmounted the large rise of pressure (fig. 42).

Movement of the recorder within the sphincter, whether inward or by rotation, induced a small peak of increased pressure (figs. 41, 42), which passed into combined rectal contraction and relaxation of the sphincter, and often defæcation. Nocuous stimulation of any part of the cutaneous area of any of the sacral segments on the right side induced a small brisk and brief contraction of the sphincter and levator ani which subsided in three to five seconds, and was often followed at an interval by defæcation (fig. 40, *a*, *b* and *c*).

Digital exploration revealed that the source of the faint jerkiness in the record was faint irregular contraction in the outer segment of the sphincter ani, in that region where the voluntary constriction of the normal sphincter is usually felt. The contraction elicited by cutaneous

stimulation of the right sacral segments also caused a faint constriction in this place. Though jerkiness could be felt in this region no distinct tonic constriction could be related to it. The sphincter relaxed slowly and contracted slowly as a whole, and the muscle giving the more rapid contractions felt as if embedded in the outer part of this slowly contracting unit, without giving distinct constriction.

Case 7.—D. McK., aged 28. Fracture dislocation of 11th thoracic vertebra with destruction of 2nd, 3rd, 4th and 5th lumbar segments and partial affection of 11th and 12th dorsal and 1st lumbar segments.

Fourteen months earlier he fell 30 ft. with immediate complete paraplegia. Incontinence of urine developed within a few days. On examination he showed weakness of the abdominal muscles below the umbilicus on both sides. Complete paralysis of lower limbs, with hypotonia, wasting and absent knee-jerks. Both ankle-jerks were present. Stimulation of the skin of the sacral segmental areas induced contraction of the external anal sphincter and levator ani, accompanied by external rotation of the thighs and plantar flexion of the great toes. All sensation lost below the 10th dorsal segment on the left side and 1st lumbar segment on the right side. Lumbar puncture revealed a complete spinal block. He suffered continual constipation. After a purgative or enema he had some warning of imminent defæcation by sense of movement within the abdomen. Any bodily movement then precipitated evacuation. No sensation of passage, and no voluntary control over it.

Distension of the rectum in this patient evoked a high degree of immediate resistance followed by fall to a low tonic level. There was readily obtained an induced wave of rectal contraction (fig. 43), and small series of subsequent waves often occurred. These waves of secondary contractions could also be readily evoked by sudden passive increase of abdominal pressure (fig. 48). The sphincter ani showed the fine jerky irregularities characteristic of slight activity of the voluntary external sphincter. Distension by small increments encountered a moderate resistance (fig. 18). Sudden brief passive abdominal pressure induced a brief contraction in the jerky portion of the sphincter (fig. 48) followed by the slower relaxation of the remainder.

The rectum when well distended showed occasional small waves of contraction at intervals of forty to sixty seconds, each accompanied by a small relaxation in the sphincter commencing at or just before the peak of the rectal wave (fig. 46). In this patient the rectum contracted powerfully with each micturition (reported as Case 5 in our earlier paper on micturition [8]), and with these contractions the anal sphincter relaxes steeply in the later phase of rectal contraction (fig. 47). It will be observed that the pressure in the sphincter rises with the onset of vesical contraction, a phenomenon related to contraction of the whole

of the voluntary muscle of the perianal perinium in the early stage of vesical contraction.

This preliminary contraction of the perineum and anal sphincter appeared to be related directly to the rising pressure in the bladder, for when the combined micturition and defæcation were elicited by repeated abdominal pressures the rectal pressure rose early, and passed into a high wave before the similar transition had occurred in the bladder (fig. 49, *b*, *c*), and the sphincter ani showed early relaxation accompanying the first rise of rectal pressure. Here the sphincter ani again contracts before defæcation occurs. The pressure in the sphincter ani was recorded only by means of a small olive-shaped rubber balloon in this patient, so that the wider movements of the involuntary anal sphincter were not clearly differentiated. Well developed reflex micturition was present, with brisk external vesical sphincter.

Case 8.—E. R., male, aged 47, under the care of Dr. Hinds Howell, intramedullary spinal tumour extending from 11th dorsal segment approximately to the level of the 1st sacral segment.

He had had gradually increasing weakness of the lower limbs for a period of eight months, with bouts of aching pain felt in the lumbar spine. Numbness and coldness of the lower limbs had existed for five months, and wasting and twitching of the lower limbs for four months. He had had constipation, and difficulty in initiating micturition for six months. There had been precipitant and uncontrollable defæcation following the administration of aperients. He had complete inability to discriminate between flatus and solid matter. On examination he showed general wasting of the musculature of the lower limbs with flaccid quadriceps and increased tone in the calf muscles. The abdominal reflexes were absent below the 9th dorsal segment. The knee-jerks were diminished, ankle-jerks exaggerated, with ill-sustained ankle clonus. Plantar responses both extensor. Anal reflex present. Almost complete loss of sensation to all forms below the 9th dorsal segment with less deep affection of the 5th lumbar and sacral segments. Sense of position and passive movement deeply impaired in toes, less so in ankle and knee joints. Loss of sense of vibration below 4th lumbar spine. Operative exploration revealed distension of the spinal cord in the region referred to above.

The rectum reacted to distension with the production of secondary waves of moderate size and showed moderate plasticity (fig. 50). The sphincter ani was resistant to inflation and at moderate distension showed slow undulating fluctuations. A single moderate distension evoked, besides the initial resistance, a small peak of contraction related to the outer segment of the sphincter, with subsequent small trough before the maintained tonic level was reached (fig. 50, *a*). The reaction to distension by small increments was not examined, but

palpation revealed that apart from the brief initial contraction the sphincter was lax.

Inflation of the rectal balloon evoked a full relaxation of the sphincter ani (as recorded by small olive-shaped balloon) (fig. 50, *c*), while progressive distension of the intervening segment brought about a slow and gradual rise of rectal pressure associated with deep relaxation of the sphincter ani. Although further introduction of fluid ceased the rectal pressure continued to rise, and superimposed smaller fluctuations made their appearance. The resulting large prolonged contraction was accompanied by parallel change in the intervening segment, and secured evacuation of fluid (fig. 51, *c*, *d*, and *e*). The sphincter remained fully relaxed (small olive-shaped recorder), and reverted to a phase of increased tone as the rectal contraction subsided (fig. 51, *f*).

Each involuntary flexor spasm, and flexion induced by stimulation of the sole of the foot, was accompanied by a sharp and brief contraction in the external sphincter (fig. 53, Plate V, *a*, *c*), and often with associated wave of rectal contraction possibly stimulated by perineal movement. The brevity of these reflexly produced contractions suggests their origin in striped muscle, and where the sphincter was already relaxed (fig. 52, *c*, *d*, *e*, *f*) their rapid subsidence left no apparent slower contraction. Each secured brief cessation of evacuation when that was occurring (fig. 52, *c*, *d*). Movement within the sphincter also induced rectal contraction and flickering contraction in the sphincter. Voluntary effort to restrain defæcation was accompanied by rapid but weak and momentary closure of the external sphincter ani not associated with change in the rectal contractions. Where spontaneous contractions of the rectum occurred they had reciprocal relationship to the slow rhythmical fluctuations of tone in the sphincter.

Involuntary powerful micturition with brisk reflex effects had developed in this patient, though he still had some ability to restrain micturition for brief intervals.

Case 9.—H. C., male, aged 60, under the care of Dr. Hinds Howell. Carcinoma of gall-bladder. Secondary deposit compressing spinal cord at level of 5th dorsal segment.

For ten weeks he had aching pains in both groins and indigestion, followed after two weeks by pain in the back. Legs gradually became weaker until six days before admission he was unable to move or to feel his lower limbs. The next day he was unable to pass water and fæces and the next lost all sensation from bowels and bladder. Catheterization was required. Enemata secured small bowel evacuation. He showed on examination complete paralysis of all muscles below the 5th intercostal. Slight extensor rigidity of lower limbs.

Reflexes: brisk knee and ankle-jerks of small range, unsustained ankle clonus. Abdominal reflexes absent. Plantar responses extensor with reflex flexion of lower limbs. Anal reflexes absent. Sphincter ani of moderate tone and plasticity. Sensation completely lost to all forms below the 5th thoracic segment.

In this patient, in whom there was commencing failure of all limb reflexes from general toxæmia at the time of our examination, the reaction of rectum and anal sphincter closely resembled those following cauda equina lesions except that the latter was highly resistant and independent. Distension of the rectum did not elicit any induced wave of contraction although the tonic level was well maintained, and distension of the sphincter encountered a high resistance (fig. 19). At moderate distension the sphincter ani showed long slow fluctuations of pressure (fig. 56), and reacted to rectal distension by only slight relaxation (fig. 56, *d*, *e*). Filling the intervening segment evoked at first deepening of the periodic relaxations of the sphincter without change in pressure in the rectal balloon, and as higher volumes were reached the relaxations of the sphincter deepened, and waves of contraction on the rectal balloon commenced to appear in exact correspondence with each such relaxation (fig. 57, *a*, *b*, *c*, *d*, and *e*). No evacuation occurred, and with further filling the rectal contractions subsided, the relaxation of the sphincter grew less, and a generally lowered tone of the sphincter appeared. Frequent small contractions of the sphincter were now observed (fig. 57, *h-k*). At other times, even with the rectal balloon well distended, there was no evidence of rectal involvement in the rhythmical fluctuation. Distension of the sphincter could excite the appearance of these small rectal waves. No reflex responses in the sphincter were elicited, and movement within the sphincter evoked no rapid contraction.

At the time of this rectal examination the bladder showed no evidence of reaction at any volume up to 1,200 c.c., so that involuntary micturition had failed.

Case 10.—P. C., aged 40, under the care of the late Dr. Collier. Fracture dislocation of 11th thoracic vertebra. Extensive damage to spinal cord from D 7 segment downwards. Residual reflex activity of sacral segments.

In 1915 he fell 38 ft. with immediate loss of power and sensation up to the level of the chest. Retention of urine for two weeks, thereafter incontinence. Power of legs gradually improved and sensation reappeared to some extent on body and right leg. In 1916 retention of urine necessitated catheterization for two to three weeks, after which he gained some ability to pass and control it. Bowels very constipated with precipitant evacuation after taking purgatives. Perforating ulcer and osteomyelitis of left tarsus for eight years. There

was slight spasticity of the extensors of both hips and knees. The calf muscles were flaccid. There was wasting of both calves and of both glutei. The abdominal reflexes were present on both sides, the knee-jerks both brisk, the right ankle-jerk present, the left absent. Both plantar responses extensor. Anal reflexes present. There was slight loss of sensation to touch, pain and temperature from D 7 to L 2 segments, and complete loss to all forms over the remaining lumbar and all sacral segments. X-ray revealed a crush fracture of the 1st lumbar vertebræ.

Distension of the rectum resulted in a moderately high rise of pressure followed by a small induced secondary wave (fig. 58), and succeeded by a slight degree of plastic adaptation. Inflation of the sphincteric recorder resulted in a high curve of pressure increase with good adaptation at high distension (fig. 20). The sphincteric record is jerky throughout, and this jerkiness was readily identified with a jerky tonic contraction of the whole voluntary musculature of the perineum. From the rapidity of the contraction and relaxation of each jerk this feature appeared to be directly referable to a slight and flickering tonic contraction of the external voluntary anal sphincter. A cutaneous stimulus to the thigh or sacral skin segments evoked an immediate rapid increase of pressure in the sphincter ani and movement of levator ani. Movement of the recorder within the sphincter, even its rotation through some 19 to 15°, resulted in a similar sudden jerk of contraction in the sphincter and rise of all pressures from contraction of the levator ani.

Distension of the rectal balloon produced a well-defined but small relaxation of the pressure in the sphincter, while distension of the intervening segment evoked well-defined relaxation (fig. 60, *b*) with slow rise of rectal pressure and later powerful and rhythmical fluctuations (fig. 61). These were associated with an earlier rise of pressure in the sphincter (fig. 61 at *d*) and relaxation beginning at or near the crest of each wave of rectal pressure (fig. 61, *e*) coinciding with the onset of evacuation. The same rises occurred with spontaneous rectal contractions, as in fig. 59.

Inflation of the recorder in the sphincter to a moderate volume resulted in a high immediate resistance, followed, after a small "hump," by a trough of relaxation lasting some fifteen seconds. A small wave of rectal contraction often appeared, and then the initial peak was followed by an uninterrupted and more prolonged relaxation (fig. 60, *a*). Insertion of the recorder also elicited a similar contraction of the rectum (fig. 58, *c*).

The bladder reacted briskly to distension and large isolated reflex

micturitions could be readily provoked at volumes of 250 to 350 c.c. The external vesical sphincter was active.

Case 11.—E. W., aged 43, under the care of Dr. Hinds Howell. Mildly spastic paraplegia of undetermined cause. Pronounced hypertonia of anal sphincter.

Progressive stiffness, trembling, weakness and coldness of right leg for eight months, and trembling of the left leg for six months before admission. Numbness around the left ankle for three weeks. Right hand shaky, dry and cold for five days. Micturition: for two months urgency and frequency with precipitant evacuation which he is unable to control. If he attempts to pass without first feeling the desire he has to strain. Severe constipation. Urging and straining necessary to get the motion into the back passage and when there it will go no further. So he presses with his finger (between coccyx and anus) and so extrudes the motion. After taking a purgative he feels desire for defæcation continually for about two days, feeling as though the bowel is loaded and should be emptied, but unable to defæcate when this was attempted. Examination revealed optic nystagmus, and impairment of alternating movements of the right upper limb. Weakness of flexion movements of both lower limbs with definite increase in tone of extensors in the right; slight increase in the left. Fibrillation observed in calves. All deep reflexes very active. Abdominal reflexes absent. Plantar responses right extensor with reflex flexion of the limb, left indefinite. Slight loss to all forms of sensation over skin segments S 3, 4 and 5, more definite right than left. Vibration slightly reduced over right malleolus. Right hand colder and drier than left, probably due to vascular causes. The cerebrospinal fluid was normal.

Though the exact nature of the nervous lesion in this patient is obscure he is included in this series on account of his possession of an extreme degree of resistance of the anal sphincter. Inflation of the rectal balloon revealed a high degree of maintained rectal tone, and large secondary waves followed each increment of 10 c.c. beyond 30 c.c. (fig. 63). These secondary waves possibly involved the whole rectum, for they appeared in the intervening segment. With 50 c.c. of air in the rectal balloon slow rhythmical waves occurred at intervals of thirty to fifty seconds. The anal sphincter was extremely resistant to distension (fig. 21), and also showed high degree of recovery of tone with each step of deflation of the sphincter recorder. When the tension within the sphincter passed 50 cm. of water, fluctuation of the pressure appeared, and in continuous record was seen to be due to spontaneous relaxations of the anal sphincter occurring at intervals of sixty to ninety seconds (fig. 63, *c*, *f*). Inflation of the rectum brought about relaxation of the sphincter only when it coincided with the appearance of one of

these spontaneous relaxations—which then became immediately deeper. In the intervals the sphincter appeared resistant to this effect (fig. 63, *a*, *d*). Passive increases of abdominal pressure were also without effect (fig. 64, *m*, *o*). Small waves of increase of pressure in the rectal balloon usually accompanied each spontaneous relaxation of the sphincter, and as these increased in size when the rectum became more active the commencement of each was seen to occur some five seconds earlier than the corresponding relaxation of the sphincter.

Progressive filling of the intervening segment with fluid brought about a gradual rise of rectal pressure surmounted by a series of slow contractile waves, and the sphincter ani relaxed more deeply when each of the rhythmical fluctuations became due (fig. 64, *g*, *i*) and at other times more slightly in accompaniment with waves of rectal contraction (fig. 64, *h*, *j*). In spite of increasing rectal distension evacuation occurred only with the first relaxation of the sphincter. Stimulation of the sole of the foot evoked only a brief phasic contraction of the sphincter (fig. 64, *b*, *g*), and any delayed effect was lacking, suggesting that only the external striped sphincter had contracted. Movement of the recorder in or out within the sphincter also evoked this brief contraction without affecting the tone of the involuntary sphincter.

The reaction of the urinary bladder to distension was depressed. A series of small waves of vesical pressure appeared at 400 c.c. and resulted in dribbling micturition. The external vesical sphincter contracted with stimulation of the sole of the foot.

V.—The Normal Rectum and Anal Sphincter.

Two normal subjects without history of nervous, vesical or rectal disorder were investigated by the method we have used in the foregoing experiments. As our findings were identical in the two they need not be treated separately.

Distension of the rectal balloon when it lay some 7 to 10 cm. above the anal sphincter, encountered an initial resistance which fell immediately the volume became constant (fig. 65, 66, 70 at *a*). There occurred a small wave of induced rectal contraction, succeeded by a fall to a low maintained tension. When sensation of desire to defæcate was present the secondary induced contraction was found to be present, but not large, and maintained tonic level high (figs. 65, 66). When such desire had been successfully postponed the rectal balloon tended to move inwards to a higher level where tonic contraction was feeble, and the secondary contraction induced by distension was faint or absent. When

moved down to proximity to the sphincter, secondary contractions again continued to be elicited, as in fig. 70. Without radiological control we are not certain of the exact anatomical relationship of this inactive region, apart from its lying beyond 15 cm. within the sphincter. With the appearance of an induced wave of contraction the pressure in the intervening segment rises concurrently (fig. 70).

The graphs of resistance of the sphincter ani to distension (figs. 22, *a*, and 23) gave low curves with well-developed plastic adaptation in most of the experiments. As we had hoped to obtain records of the pressures during evacuation of fæces, desire for defæcation was present at the time of distension. Under other circumstances the curve is much higher, so that the later part of the manometer tracing passed beyond our recording paper (fig. 22, *b*). No slow rhythmical fluctuation was observed at any level of distension. The reaction to sudden moderate distension took the form of a sharp peak followed by relaxation, which has a "hump" of late contraction before reaching a maintained level (fig. 10). It is without the high initial resistance of the sphincter of spastic lesions, or the rhythmical later rise of the cauda equina lesions.

The character of the record differs markedly according to the portion of the sphincter ani most related to the recorder. If, for instance, the recorder is moved from within the rectum outwards in a series of steps, the first rise of pressure as intrarectal pressure ceases to be recorded is smooth in general outline, and pulse beats are observed on it (fig. 65, *a* to *b*). When the recorder is moved 1 cm. further out, the pressure rises, but the general characteristics of the curve are the same (fig. 65, *b* to *c*). One cm. further out the rubber portion begins to become visible externally, the pressure rises a little higher, and the tracing presents small irregular jerkings (fig. 65, *c* to *d*). On moving it still further out, the pressure falls slightly (fig. 65, *d* to *e*), and then the record becomes irregular and jerky and requires to be held rigidly to prevent its extrusion (fig. 65, *e* to *f*). The jerkiness is much less obvious if the subject is lying supine, and is then found to become reasserted with any abdominal movement. In the lateral posture it may readily be ascertained by digital examination to be exactly related to the small ring of muscle which contracts during voluntary restraint, the external voluntary sphincter. The small jerky contractions are found to be a tonic contraction of this sphincter, associated with tonic contraction of the pelvic floor in fulfilling the function of tonic regulation of intra-abdominal pressure. Thus the movement of a limb, necessitating some fixation of the trunk, immediately throws the pelvic floor and the external

sphincter ani into contraction (fig. 68). It may also be observed that this sphincter, which lies distinctly external to the tonic portion of the sphincter ani, is in general not contracted, though readily thrown into maintained contraction by the synergic movement above mentioned, or by voluntary effort. A sudden moderate distension of the recorder when related to the outer portion of the sphincter ani elicits a large jerk of contraction in the external sphincter, but the subsequent relaxation of the curve is that of the internal sphincter with the superimposed irregular contractions (fig. 11).

Sudden distension of the sphincter or movement within it stimulates a rapid momentary contraction of the levator ani as well as of the external voluntary portion of the sphincter. No contraction of the rectum was observed to be stimulated. Inflation of the rectal balloon, on the other hand, induced a well-defined relaxation of the inner tonic sphincter (fig. 69) in all other respects identical with type with that seen after lesions of the cauda equina. If the sphincter recorder be further out, and registering some jerky contraction of the external sphincter, inflation of the rectal balloon then evokes but faint relaxation (fig. 66, at *a*) attributable to the portion of the recorder still compressed by internal sphincter, while the twitching external sphincter remains unaffected. The relaxation of the internal sphincter produced by a given inflation of the rectal balloon was greater if desire for defæcation were present, and absent if the rectal balloon had moved high in the rectum. The internal anal sphincter is found to show this type of relaxation after an effort to defæcate by straining (fig. 73), and following the sudden rise of abdominal pressure during a cough.

Distension of the intervening segment with a small amount (20 c.c.) of fluid results in rapid and prolonged relaxation of the internal sphincter, and with only slight and mainly passive rise of rectal pressure (fig. 71). If the filling is progressive and the rectal balloon previously inflated, automatic defæcation occurs (fig. 74). The subject is aware of imminent defæcation, and if he does not influence it by straining, a series of large waves of rectal pressure, with small relaxations of the sphincter accompanying them, occurs (fig. 74). These relaxations show reciprocal relationship with the rectal contractions. The jerky external sphincter continues irregular twitching throughout the relaxation. An occasional larger involuntary twitch of the perineum is superimposed as at *b*, fig. 74.

Voluntary restraint of evacuation was seen as an abrupt contraction of the external sphincter. On one occasion, shown in fig. 75, the rectal

contraction subsided during the onset of voluntary contraction of the external sphincter, and following cessation of the restraining effect there was very little further evacuation and no further rectal contraction. The wave shown here was the last of a series of such waves evoked by distension, identical in shape with the others, and the rectum had been emptied by the evacuation, so that we do not believe that it has been unduly curtailed. Even when the effort was prolonged for some thirty seconds, there was never observed any direct damping of the rectal contractions, which would subside gradually after continuing for a considerable period. They subside in similar fashion if the rectal contractions are not sufficiently strong to overcome the obstruction of the sphincter by the recorder. Voluntary restraint is also without effect on the internal sphincter, for immediately a restraint is relaxed the tone of the internal sphincter is found to have continued its activity before the restraint (as in fig. 74 at *g*). Voluntary effort to defæcate without abdominal contraction was completely without effect on the rectum and internal anal sphincter, even when on one occasion some 250 c.c. of warm fluid had been run into the intervening segment (fig. 76*c*). That this procedure, though bringing no sensation to the subject, was not without some effect was shown by the finding that sudden distension of the rectum now induced an exceedingly brisk contraction of the rectum, and relaxation of the sphincter had become exceedingly brisk, whereas before they had been sluggish.

The solidity of normal fæces renders pressure observations during normal defæcation difficult to obtain. On one occasion spontaneous defæcation after colonic distension was recorded and rectal contractions and relaxations of the sphincter similar to those obtained by filling the intervening segment were seen, but the waves of rectal pressure reached well over 120 cm. and the passage of solid fæces disturbed the placing of the balloon. A brisk terminal contraction of the levator ani is an interesting feature. The passage of flatus is also accompanied by a similar series of events, though the rectal pressures were often very high indeed (over 150 cm.). Waves of rectal contraction were also observed during micturition but were not associated with any relaxation of the sphincter ani.

VI.—The Peripheral Autonomy of Defæcation following Destruction of Sacral Innervation.

Following accident or disease which brings destruction of the 2nd, 3rd and 4th sacral motor roots on both sides all evidence of any capacity

of *rapid* contraction or relaxation in the sphincter ani vanishes. The reactions which we have observed and figured in Cases 1, 2, 3, and 4 are extremely slow in both increase and decrease in tension. There is no apparent effect of voluntary effort to relax or contract the sphincter, and stimulation of the skin is without result. The highly sensitive and rapidly contracting external voluntary sphincter is not in functional evidence. Arloing and Chantre [1, 2] and Elliott [9] have described the slowness with which this muscle loses its striation following deprivation of its motor nerve supply. They further find that response to faradic stimulation remains indefinitely after such degeneration. As it is also described that such contraction in response to faradization, having commenced at one point, spreads to the musculature of the whole perineum [9] it appears very likely that this persistent feature is related not to the striped musculature, but to the involuntary muscle and closely related autonomic plexus which is intimately mingled with the fibres of the external sphincter (Roux [32]), and invests the whole pelvic floor. There is no evidence that the external sphincter remains tonic. We have in Case 2 observed in correspondence with relaxation of the anal sphincter, a relaxation of the surrounding pelvic floor with exactly similar slowness of duration. We therefore believe that, while the striped portion of the anal sphincter may be slow to lose histological structure as a result of nerve lesions, it plays no part in the reaction of the sphincter in these cases.

We may conveniently first consider the "tone" of the non-striped, involuntary anal sphincter, as seen in the cases of lesion of the roots of the cauda equina. Sherrington [35] has defined the general nature of the postural tone of muscle as a reaction to stretch, and pointed the application of this generalization to such phenomena as adaptation of the urinary bladder to the volume of its contents. This property of adaptation in the case of the bladder, originally described by Mosso, we have ourselves observed [7, 8], and found that increasing tension excited increasing contraction of the detrusor musculature, while constant tension excited less contraction. Increase of tension is a more powerful stimulus than constant tension. Following increase in volume an adaptation of posture, with fall of internal pressure, is therefore the direct result of lessening of the stimulating value of stretch. With gradual increase to large volume of vesical content the contractions of the detrusor also tend to fluctuate, and here a further factor of periodic voluntary and involuntary suppression of the vesical reaction occurs and complicates the fundamental postural tonic reaction. Nevertheless at

such volumes, and to less degree at smaller volume, a sudden powerful increase in tension is followed by transitory depression of subsequent postural tone, so that tension as a stimulus may have directly opposed effects.

The reaction which the sphincter ani presents, following sudden moderate increase in the volume of its content, takes the form of a sharp initial peak of increased pressure followed by a rapid relaxation to a low pressure for ten to twenty seconds, followed in turn by a gradual rise to a higher level (figs. 3, 7, 26). The later rise usually shows superadded small fluctuations at intervals of five to ten seconds which fade gradually, leaving a residual steadily-maintained pressure, which is the postural tone of the muscle. Immediately the initial resistance is overcome, adaptation to the fresh tension has commenced by a relaxation followed by increase of tone. This form of curve was constantly present in the sphincters of patients with cauda equina lesion, and the early relaxation and later development of tonic contraction are readily palpable on digital exploration of the sphincter. Momentary passive increase of tension induces the same early relaxation although the volume is not changed for more more than two seconds (figs. 4 and 5). These changes, consequent upon distension, may therefore be related directly to a momentary resistance of the involuntary muscle to a sudden stretch, followed by a maintained contraction of the muscle upon its contents. Some small part of this general reaction is certainly due to the purely visco-elastic nature of the tissues concerned, but that the remainder is an expression of active muscular contraction is clearly demonstrated by two further reactions. These are, first the ability of changes at a distance to induce momentary and almost complete relaxation, and secondly the spontaneous and often rhythmical fluctuations in the resistance of the sphincter. Such passing fluctuations form no part of the reaction of non-contractile tissues.

The relationship between the amount of distension of the sphincter and the level of residual maintained contraction and the relationship of this to the degree of initial resistance is illustrated by plotting both these pressures for each 1 c.c. of distension of the recorder. It will be observed (figs. 12 to 15) that both pressures increase with increase in volume of content of the recorder. After a certain degree of distension the adaptation after each increment of distension is such as to maintain the resistance within comparable level over a wide range of distension. Between volumes of 5 and 20 c.c. in our recorder the pressure exerted by the sphincter is largely " plastic " and adaptive. From case to case

wide differences are seen, so that this adaptation takes place at a much higher level of pressure in Case 1 than in Case 4 and this higher than in Case 3. Comparable differences in general resistance of the sphincter are seen in the same patient, as in Case 2 (fig. 13, *a* and *b*), here being determined by distension of the urinary bladder. Palpation of the sphincter showed that lowness of the curve reflects that softness of the sphincter commonly called "patulous" (though not actually gaping), and that this condition of resistance is by no means constant in cases of cauda equina lesion.

The reaction of the sphincter ani to sudden distension is, therefore, twofold, an immediate relaxation, and a delayed re-assertion of tonic contraction. The latter is presumably present from the commencement of distension, but at first is overshadowed by the former. There is evidence [34, 6] that the postural tone of striped muscle is an equilibrium between exitation and inhibition, both induced by tension on the muscle, and that when a sudden increase of tension is made the latter predominates, giving rise to the "lengthening reaction." The anal sphincter presents, therefore, a directly comparable reaction, though in the patients here considered the central nervous system does not appear to be concerned. A sudden reduction in content is followed by gradual restitution of tonic contraction at a fresh level of length of muscle fibre (fig. 6) directly comparable to the "shortening reaction" of striped muscle. The posture for the sphincter is determined by tension upon it and stretch is the adequate stimulus for postural "tone."

Sudden inflation of a balloon within the rectum by a small amount of air is accompanied by an immediate rise of pressure within the balloon followed by commencing sharp relaxation to a lower level of maintained contraction. Further sudden increment of volume in the balloon results in further sudden rise of pressure, followed by a slow wave of contraction commencing within two seconds after the distension, so that the eventual resumption of a slightly higher tonic level is delayed. Additional increments in volume excite larger induced waves of rectal contraction. Where the pressure of fluid in the segment intervening between rectal balloon and anal sphincter was recorded as well, it was evident that, apart from slight effects transmitted directly from the balloon to the fluid, the rectal wall of the intervening segment participated directly in these induced waves of pressure upon the rectal balloon when they were large. With small responses only the distended segment showed the contractile wave. There was no evidence of fluctuation travelling towards the anus from the distended region. The

residual level of maintained contraction at the level of distension, as in the sphincter ani, increases in proportion to the degree of distension. A segment of the rectum, therefore, reveals a comparable postural relationship to that of the sphincter, except that the phasic disturbance induced by sudden distension begins, not with relaxation, but with a wave of contraction when postural tone is high. The wave of contraction may under these circumstances also be induced with ease by a momentary increase of tension such as a transient pressure through the abdominal wall, and its latency, then more accurately estimated, is found to be 1·2 to 1·8 seconds from the onset of increased tension. Any inhibitory effect derived from stretch of the rectum is not evident, as also is the case in similar waves induced in the urinary bladder [8]. The induced wave of rectal pressure was more readily obtained when the balloon was low in the rectum (*cf.* Case 2), but the movement of the balloon may have altered the condition of the whole rectum. At times the wave was obtained when the balloon was thought to be very high. The maintained level of postural tone in both rectum and anal sphincter presents fluctuations. Some of these are in the form of brief waves at short intervals, and these usually occur when the tonic contraction is settling down to a fresh level following some induced change, as in fig. 26. Others are in the nature of slow fluctuations at long intervals, more commonly seen in the sphincter ani and elicited by full distension. They occur in the sphincter when the rectum is empty, and when the rectal balloon is distended fully the more frequent waves of pressure observed in it are enhanced in size in the phase of relaxation of the fluctuating sphincter. The fluctuations in the sphincter can occur without evidence of parallel changes in rectal pressure.

In 1877, Gowers [15] published a series of observations on the behaviour of the sphincter ani in two cases of transverse lesions of the spinal cord and one complete lesion of the cauda equina. He recorded the contraction of the sphincter in response to insertion of a hollow rubber recorder, and in response to inflation of the rectum with air, and demonstrated the fall in tone of the sphincter after the latter procedure. He found no difference in the two types of lesion, so that it is surprising to find in all the editions of his later book [16] the statement that "if the lumbar centre is inactive there is momentary contraction and then permanent relaxation" of the sphincter in response to its distension. With the later statement we are unable to agree.

Distension of the intervening segment with fluid, the rectal balloon and sphincter recorder being already moderately distended, resulted in

the appearance of an isolated rise in rectal pressure, or a premature larger rise if spontaneous fluctuation has been occurring. Immediately the inflow is ceased the pressure within the intervening segment is itself found raised. Later development of the wave in the balloon possibly represents ascending spread of contraction from the locus of distension, as in fig. 26 at *m*, *n* and *o*. Such evidence of progressive contraction is rare, and most usually rhythmical contractions once set up occur contemporaneously in the region of rectal balloon and the fluid in the intervening segment. We have not experimented with two separate balloons, which would perhaps reveal travelling waves of contraction more frequently.

Distension of the rectal balloon induces a deep relaxation of the tone of the sphincter. The presence of a wave of contraction in the rectal segment which is distended is attended by deeper relaxation of the sphincter, but is not essential for its presence. Movement of the balloon within the rectum also induced relaxation of the sphincter, but deflation of the rectal balloon is without any effect. This reaction becomes more striking if a wider area of rectal wall be subjected to tension by the introduction of fluid into the intervening segment. There then ensues a contraction in all segments of the rectum recorded, with deep relaxation of the sphincter, and fluid is evacuated. Continued introduction of fluid results in the appearance of regular fluctuations in rectal pressure with reciprocal relaxations of the sphincter (figs. 2 and 33). Intermittent evacuation may become continuous in the full development of this reciprocal process, by partial fusion of the waves of rectal contraction.

The reciprocal relationship which holds between rectum and anal sphincter is therefore the basis of a mechanism which can secure co-ordinated evacuation. The series of events seen in fig. 2 appear to us adequately to constitute the performance of the automatic co-ordinated and intermittent defæcation readily observed to occur in these patients. The stimulus for its occurrence is distension of the rectum, and sufficient relaxation of the sphincter to allow some passive evacuation of fluid under its own pressure does not occur unless active reciprocal contraction of the rectum provides the driving force of the reaction. For the evacuation of solid fæces more powerful contraction of the rectum would appear necessary. The presence of contraction of the rectum in reponse to distension of the rectal balloon in Case 2, with lack of powerful rectal contraction when the intervening segment was distended, is interpreted as evidence of imperfect and partial development of automatic defæcation.

Automatic defæcation in patients suffering from destruction of the

sacral innervation of the rectum appears to be the counterpart of that described in animals where the sacral segments of the spinal cord have been destroyed [14], and also where the more extensive destruction of cord has removed the connection of the rectum and sphincter with the nervous system via the sympathetic nervous system (hypogastric nerves) [27]. The remaining nervous mechanism is that peripheral ganglionic plexus related to the wall of the rectum. The reciprocation between rectum and sphincter which we find to be induced by inflation of a segment of rectum at a distance from the sphincter appears to be of necessity nervous in origin. As with the similar reciprocation observed in the reaction of automatic micturition [8] the nervous mechanism concerned requires a peripheral sensori-motor reaction of reflex kind, foreign to the conception of the sympathetic nervous system as a purely efferent system. That such a peripheral "reflex" is not altogether beyond possibility in relation to parasympathetic ganglia is demonstrated by similar phenomenon of the myenteric reflex in the intestine. In invertebrates smooth muscle without nervous tissue is stated to react to stretch by contraction [4] and propagated waves of contraction are observed in intestine subjected to the action of nicotine [36], so that the postural tone described in the rectum and sphincter cannot with certainty be described as of nervous origin. Nevertheless, the spontaneous concurrent rhythm of fluctuation without phase difference in different parts of the sphincter, and the relaxation of the sphincter brought about by distension of a distant portion of the rectum necessitate the integrating activity of a peripheral nervous plexus.

VII.—The Regulation of Defæcation by the Central Nervous System.

Whether the rectum and sphincter are innervated by the rectovesical plexus alone, or with the addition of reflexly active spinal segments, or in full communication with the whole nervous system, a simple automatic co-ordinated reaction may in them be demonstrated. A rapid increase in the rectal content is followed by a passing fall of tone in the sphincter. A slower but progressive increase of rectal content leads to its actual evacuation of rhythmical contraction of the greater part of the rectum, and more prolonged and rhythmical relaxation of the sphincter.

Both these reactions, of which the first is but a fraction of the second, we have demonstrated in the rectum deprived of sacral innervation, these forming the basis of the clinical phenomenon of "automatic

defæcation." Their form when the rectum and sphincter are controlled by the central nervous system appears to have undergone only quantitative change; the mechanism of these reactions still may be regarded as local. The integrity of the spinal and central pathways, though not essential for the performance of elementary automatic defæcation, has nevertheless a certain degree of influence upon it. The approach of the analysis of these effects appears most readily to be made in first considering alterations in the postural tone of the rectum and sphincter, and later the phasic reactions to passing stimuli.

The Postural Tone of the Sphincter Ani and Rectum.

Digital palpation of the sphincter ani evokes a much greater initial resistance in cases with intact sacral innervation than where a lesion of the cauda equina has destroyed this innervation. Such examination is imitated by a sudden moderate distension of the sphincter recorder, and the additional resistance of the former cases is seen in such records as a high initial peak followed by a "hump"-shaped initial delay in relaxation (figs. 8, 9 and 10). The high initial resistance is here, by digital exploration, readily identified with the presence of momentary contraction of the external voluntary sphincter in response to movement within the anus (figs. 38 and 65). When this initial brief resistance is passed some delay in further relaxation is appreciable to careful digital examination. It is variable in degree of development and appears to be a slow wave of contraction in the involuntary portion of the sphincter which obscures the earlier portion of a relaxation, which otherwise resembles that observed in cases of cauda equina lesion. This "hump" of delayed contraction was more prominent when associated with a higher curve of reaction to gradual distension (*cf.* Cases 6 and 9). If our surmise that the postural tone of the sphincter is an equilibrium between relaxation and contraction, both induced in the sphincter by tension upon the muscle, be correct, the appearance of the hump of induced contraction in "hypertonic" sphincters may be interpreted as enhancement of the excitatory element. It was observed in the sphincters of cases of cauda equina lesion when highly tonic.

Gradual distension of the sphincter by small increments does not elicit either contraction of the external sphincter or the hump of delayed relaxation, and is therefore a more true measure of the degree of development of postural tone. Comparison of the graphic representation of resistance of the sphincter in states where the sacral segments are reflexly active (Cases 6 to 10, figs. 16 to 21) with those seen after cauda

equina or conus lesions (Cases 1 to 5, figs. 12 to 15) reveals no obvious and constant feature of difference in maintained postural tone. The reaction of the sphincter in any one case usually remained within comparable limits for the duration of our experimental investigation, and on the occasions when the same patient was examined on different days. Occasionally we found changes during the experiment which strongly suggest that over periods of several hours fluctuations of state were occurring. The different shapes of curves may therefore over-emphasize transient, but slow, differences. We have found two causes of such variation, the one being distension of the bladder, the other distension of the upper rectum and probably pelvic colon. We have already commented upon the rise in postural tone in the sphincter in Case 2, resulting from relief from distension of the bladder (fig. 13), and the raised tone of the sphincter immediately following evacuation of the rectum may be indicated (figs. 34, 52 and 62). In Case 9 it will be observed that whereas continued inflow of fluid into the intervening segment elicited at first deepening of the relaxations of the sphincter and the appearance of rhythmical contractions of the rectum (fig. 57, *a* to *g*), these changes later subsided and the sphincter adopted a general lowering of tonic contractions. By this time the large volume of fluid injected, the abdominal discomfort of the patient, and gurgling sounds within the abdomen gave evidence of distension of the distal colon. The initial response of automatic defæcation had here given way to a passive state allowing retrograde distension of the colon, associated with a lowered postural tone of the sphincter. The reverse of this change is illustrated in the experiment on Case 6, in whom a soft "patulous" sphincter became extremely resistant following the evacuation of a very large amount of soft fæces (fig. 17, *a* and *b*). The rectum remained still partly distended, even when the sphincter became more resistant, and therefore distension of the pelvic colon might be in part presumed responsible for the earlier low curve. The lowness of the curve in Case 5 is also probably in greater part due to distension of the lower bowel. So also the resistance of the sphincter of the normal subject to distension was sometimes very high when there was no desire for defæcation (fig. 22, *b*). Garry [11] has demonstrated that, in the cat, movement in the pelvic colon evokes relaxation of the rectum and anal sphincters, and that this effect is abolished by section of the pelvic nerves or by a spinal anæsthetic. Such abolition in an acute experiment does not, however, establish the effect as a spinal reflex, and, as has been described above, the cases of cauda equina lesion after subsidence

of spinal shock reveal a similar reaction from the upper rectum. In our own experience, laxity of the anal sphincter appears to be the tonic effect of continued colonic distension of moderate degree. The effect is certainly more active in the cases of transection of the spinal cord. The resistance of the internal sphincter therefore reflects the degree of distension of the lower bowel and rectum.

Apart from these transient changes there appears to be a more durable phenomenon to be associated with "hypertonia" of the sphincter. This is an increased resistance of the sphincter to the relaxing effect of sudden rectal distension, reaching greatest development in Cases 9 and 11 (figs. 56 and 63). In Case 11 this tightness of the sphincter had become a leading complaint of the patient. The high curves in both these patients (figs. 19 and 21) might appear to represent therefore not a transient state of evacuation of the distal bowel, but a "hypertonia" of the sphincter persisting in spite of distension of the rectum. Parallel with the lessening of the effect of sudden distension of the rectal balloon upon the sphincter, there was deficiency and delay in the manner in which the sphincter relaxed and the rectum contracted in response to distension of the intervening segment with fluid in these two cases. In Case 9 this can be attributed to the poor reaction of the rectum resulting from failure of the spinal reflexes. In Case 11 good immediate contractions were obtained by sudden distension of the rectum, but without effect on the sphincter, though the reaction to progressive distension was also poor. The obscure character of the spinal lesion in this case, revealing some evidence of intramedullary damage to the conus medullaris, is unsatisfactory for close analysis. We have included it in the present series to demonstrate the extreme example in our experience of hypertonia of the sphincter. Reflex activity in the voluntary musculature in this case was slight, so that it does not appear possible to relate the tonic resistance of the sphincter to undue reflex enhancement. Such a state differs from the others only in degree, for the reaction of the rectum to general distension is poor, while reaction to inflation of one segment remains good. This dissociation resulting from partial degree of recovery has been seen in Case 2, resulting there from a lesion of the cauda equina.

It becomes clear that it is in conditions where the rectum is capable of active contraction, and is distended, that the internal anal sphincter is of low tone, extremely plastic, and soft to digital exploration. In the same cases evacuation of the rectum, of the bladder, or of the pelvic colon, brought about a return of high tone to the anal sphincter; there

is then no obvious difference from one type of lesion to another. So also the sphincter of the normal subject may be as patulous as that following complete cauda equina lesion if the subject has desire for defæcation. The tone of the sphincter ani reflects the degree of activity of the rectum at the time of examination, but its essential and particular mechanism remains identical whatever the nervous lesion. The commonly "patulous" sphincter of cases of established transverse spinal and cauda equina lesions is therefore the clinical sign of the dyschezia from which they suffer. The mechanism of the tone of the sphincter is independent of the central nervous system.

The spontaneous fluctuations at long intervals which characterized the high tone of the sphincter ani, as in Cases 1, 9 and 11, had no corresponding rhythm of fluctuation in the rectum until the latter was well distended. If the sphincter were not distended no corresponding rhythm appeared in the rectal balloon even at high pressure. The propagation and reciprocal nature of the dominant rhythm convince us of its nervous origin, and illustrate in our view that that portion of the hæmorrhoidal plexus which governs the sphincter ani here dominates the remainder. Rhythmical contraction of this kind has been observed frequently in the sphincter of the spinal animal in response to the introduction of a foreign body (Goltz [13], Sherrington [33], and Ott [30]).

Although the reaction of the rectum to sudden or progressive distension undergoes notable changes, its tone or maintained reaction to different degrees of distension is within close limits in all cases examined. The presence or absence of spinal reflex activity does not appear to be associated with any change in the postural tone of the rectum.

Spinal Reflex Activity.

In states of high tonic activity of the anal sphincter the reaction to distension of the rectal balloon, believed to be a fraction of "automatic defæcation," is less readily obtained. It might appear to be hampered by an undue tonicity, or heightening of the reaction of the sphincter to distension. We have found the condition to be a reflection of a state of rectal inactivity which appears to be the result of incomplete recovery from the initial effect of the spinal lesion, and not related to the level of the lesion.

On the other hand reflex activity of the sacral segments of the spinal cord brings qualitative additions to automatic defæcation. In the first place the response to gradual progressive distension of the rectum

develops more slowly, and takes the form of a more prolonged rise of rectal pressure, surmounted by smaller waves. This larger contraction is accompanied by similar prolonged and deep relaxation of the sphincter ani. This type of response, seen in figs. 51 and 61, often will not develop until some 800 to 1,000 c.c. of fluid have distended the lower colon as well as the rectum, though the lesser grades of distension excite small waves of rectal contraction and corresponding relaxation of the sphincter. The mechanism of rectal contraction here possesses an inertia which delays its commencement but increases its eventual force. This delay in development closely resembles the similar manner in which the bladder of reflexly active spinal states begins to react to a larger volume than that following cauda equina lesion. It would appear that spinal connections mildly checked the local automatic activity up to a point beyond which a reinforcing activity appeared.

Besides this change in the nature of the response it was found that when the rectum was but slightly distended a variety of stimuli were capable of evoking this more massive reaction. Sudden passive increase in intra-abdominal pressure, movement within the sphincter and to a less degree within the rectum, and nocuous stimulation of the skin of the sacral segments were found to be effective as provocative stimuli. The first of these by increase of intra-rectal tension may be regarded as of the same order as increase of rectal content, and reveals that passive stretch is the adequate stimulus to excite the more powerful and integrated defæcation seen in these patients. We regard this co-ordination of defæcation by the spinal segments as "reflex defæcation," and comparable to the spinal co-ordination of "reflex micturition" as we have defined it in the urinary bladder [8]. The definition of this type of rectal response from the less fused contractions of well-developed automatic defæcation resulting from cauda equina lesion is the ability of a very high rise of pressure to emerge slowly at an interval from a previously induced small active contraction without further stimulus, as in figs. 49, 51 and 37. The rectal contractions of the simple automatic defæcation of cauda equina lesions show almost comparable degree of fusion of small waves when well developed (fig. 33) though reaching lower maximal pressures (40 to 60 cm. water) compared with those of "reflex defæcation" (60 to 100 cm. water pressure). We may compare these pressures with those of 100 to 200 cm. water pressure in the rectum in the course of normal defæcation, even of fluid.

A wave of rectal contraction in Cases 1, 2, or 3, once evoked, subsided following cessation of the stimulus, whereas in the presence of

" reflex defæcation " a wave of rectal contraction set up by some stimulus tended, even if small, to progress slowly to full development of the act in spite of early cessation of the stimulus. This " explosive " character appears to require the same type of autogenetic mechanism we have postulated for " reflex micturition " [8]. The necessary pre-existence of active contraction is not so clearly defined in the case of the rectum as in the bladder, but a quantum of rectal distension is certainly necessary and is provided in the period of cumulative effect (fig. 49). It appears possible that the failure of the forceful reaction to filling of the whole rectum in Case 11, in spite of the presence of well-defined reaction to local distension of the rectal balloon, was due to the partial lesion of the sacral segments. The spinal mechanism had, so to speak, retained a general control of the rectum but was unable to effect the transition from automatic evacuation to reflex evacuation.

Stimuli applied to the sacral skin segments facilitate the appearance of this reflex response at a lower volume of distension in the same manner that they facilitate micturition. Their potency increases as the anus is approached, so that movement within the sphincter is more potent than stimulation of the skin near the anus, and the latter in turn more potent than stimulation of the sole of the foot. Well-defined reflex flexion evoked by scratching any area outside the sacral skin segments, such as the anterior surface of the thigh, was in our experience without effect in evoking this reflex facilitation of defæcation unless it produced an associated abdominal contraction which sufficiently increased rectal tension indirectly.

All the stimuli which evoke reflex facilitation of defæcation also evoke momentary sharp contraction of the external anal sphincter, and of the levator ani (" the anal reflex "). This movement is sufficiently short in response to brief stimuli to disclose the absence of any accompanying change in the involuntary internal sphincter (figs. 52 and 64), though if the latter be contracted upon some object in its lumen a relaxation commences, probably due to movement upon the object (fig. 53).

The cases presented illustrate a series of stages of development of automatic and reflex function of defæcation. The reactions of the peripheral plexus are essential to the development of spinal reflex function. On the other hand failure of reflex function from any cause appears to be followed by redevelopment of depression of the peripheral mechanism with later emergence of automatic defæcation. In all these respects, as in the general features of each state, the behaviour of the rectum follows closely that of the detrusor vesicæ. Thus, in the series of cauda equina

lesions Case 3 presented the greatest development both of automatic micturition and automatic defæcation, while Case 1 had both functions moderately developed. In Case 2 only small waves of contraction could be evoked in both rectum and bladder, and evacuation from either organ was chiefly by passive pressure past the minor degrees of relaxation which were reciprocated in the sphincters. In the cases when reflex activity was present in the sacral segments parallel development of both was seen in Cases 5, 6, 7, 8 and 10, with partial failure of both in Cases 9 and 11.

In a previous communication upon nervous disturbances of micturition [8] we included concurrent contraction of rectum and bladder when that occurred as a result of distension of the bladder, as a feature of reflex activity of spinal segments. We have now encountered a case (Case 3 of the present series) where this association occurred in conditions where spinal motor influence over the vesico-rectal plexus appears to be entirely lacking. In this patient such contraction of the rectum was accompanied by evacuation from the anal sphincter (fig. 34), as in those patients in whom there was associated reflex defæcation. In Case 7 this phenomenon was investigated in detail and the early reflex contraction of the perineum and external anal sphincter (figs. 47 and 49), commencing with the beginning of rise of vesical pressure, is notable. It was absent in Case 3. Relaxation of both anal sphincters is secondary to the development of rectal contraction. Contraction of the rectum, associated with micturition in Case 3, and in the normal subject, is seen in the form of isolated or poorly fused wave complexes in the rectum. Defæcation in response to distension of the rectum did not in these patients evoke vesical contraction even when the bladder was distended. The reaction of the bladder to distension is therefore associated with concurrent enhancement of the reaction of the rectum to distension by an activity related to the peripheral plexus. Automatic micturition has a peripheral linkage with contraction of the rectum ; a phasic aspect of the effect of vesical distension in lowering the tone of the sphincter ani. In the spinal animal fully recovered from spinal shock the occurrence of defæcation is associated with a suitable posturing of the hind-limbs and tail [33], a possible explanation of the abduction of the human limbs in the course of the "sacral reflex" (which includes the "anal reflex") seen in Case 7 and commented upon in a previous paper [8]. In a personal communication Sir Charles Sherrington has informed us that in the spinal animal micturition, if in progress, is frequently postponed with the appearance of defæcation. The lack of occurrence of micturition

in response to distension of the bowel may therefore be due to direct suppression.

We have found reason to suppose that the portion of the peripheral nervous mechanism which regulates the tone of the sphincter may dominate the rhythm of the whole rectum. Each fluctuation in such spontaneous activity has, when well developed, the same time relations as that which is apparently stimulated from the rectum. Each single wave of such reciprocal activity appears to bring contraction of the rectum as a whole, commencing a few seconds before the onset of the corresponding relaxation of the sphincter. This relationship in time is seen when such spontaneous single waves occur in full development, whether the lesion be of the cauda equina (figs. 2, 33 and 34) or above the sacral segments (figs. 45, 46 and 64), and also in the normal subject (fig. 74). Where the external voluntary sphincter is highly active each such single spontaneous contraction is preceded by a brief jerk of contraction in the sphincter (figs. 59, 62 and 74 at *b*). These same patients also exhibit the larger and longer complete reflex defæcation of which these single waves are then but a fractional form. The duration and intensity of the reaction depends on the intensity of stimulus. In the more powerful reaction a preliminary contraction of the perineum, probably also of the levator ani and external sphincter, frequently appears as the first incident in defæcation. Where a combined response of defæcation and micturition was elicited by distension of the bladder in reflexly active states, the rectum being already partly distended, this early contraction of the external sphincter and retraction of the posterior perineum is especially remarkable (*cf.*, figs. 47, 59 and 61) and may overshadow the relaxation of the internal sphincter as in fig. 62. The anterior portion of the perineum has not been found to contract at this time [8] and the earlier relaxation of the external vesical sphincter indicates that the contraction involves this muscle slightly if at all. The internal anal sphincter does not share the early contraction, which is therefore absent following lesion of the cauda equina. Sir Charles Sherrington has informed us that a brief and forcible contraction of the abdominal wall is frequently observed as an early event in defæcation in the spinal dog with high thoracic transection. None of our patients had a sufficiently high level of reflex activity to include movement of the abdominal wall, but it appears likely that the early contraction of the perineum referred to above is part of the movement which reflexly obtains a rise of abdominal pressure at the commencement of the act.

The external anal sphincter, by its rapid contraction, effects the

appropriate cessation of defæcation during the phasic spinal flexion reflex, and it appears justifiable to expect more prolonged closure of this sphincter to be an integral part of more persistent spinal reflexes such as those of progression. In the normal subject this sphincter, in close association with activity of the levator ani, has frequent synergic activity in concurrence with the abdominal musculature. An increase of abdominal pressure excites this active closure, except during defæcation, when the automatic process in the rectum and internal sphincter appear reflexly to facilitate its relaxation. It must be insisted, however, that the primary event stimulated by rise of abdominal pressure is contraction of the rectum. The external anal sphincter, therefore, functions in reflex co-ordination as does the striped external vesical sphincter. There is no evidence that it is maintained in closure in the intervals between evacuations. Palpation with the finger gives the impression of a constricted ring at the site of the external sphincter only during an effort to hold, or during a flexion or other reflex which closes it. At other times, and even during effort which secures its contraction in synergy with the abdominal wall, it can be felt to give irregular flickering contractions which feel to be carried in the substance of the tonic involuntary sphincter rather than forming a separate tonic constriction. Apart from brief retractions at the onset and termination of defæcation activity of the levator ani is difficult to define exactly owing to its mobility. It does not appear to have sphincteric function.

Micturition is subject to a central nervous influence of such kind that deep and prolonged depression of function accompanies the onset of the condition of spinal shock. In this condition the internal vesical sphincter presents maintained closure. Such a state is not obvious in the anal sphincter in the same patients, although inactivity of the bowel, with associated tympanites, is a well-known transient phenomenon. We are indebted to the kindness of Mr. Harold Wilson in allowing us to investigate the following case under his care in St. Bartholomew's Hospital at this stage.

Case 12.—Fracture dislocation of spine, spinal cord severed completely at level of 10th dorsal segment. Spinal shock.

H. R., male, aged 60, fell 12 ft. on January 14, and lost all sensation and power of movement below the waist immediately. On admission to hospital the same day there was found a complete flaccid paraplegia with loss of sensation to all forms up to the 9th dorsal segment on the right side, and the 8th on the left. There was retention of urine for which a catheter was tied in. Stimulation of the sole of either foot induced a slow flexion of the great toe on

that side, but no other effect. No other reflex response of any kind was elicited below the level of the lesion. The abdomen became very distended the next day and enemata had no result. On January 16, 1 c.c. of pituitrin was injected hypodermically without result, and this was repeated twice on the 17th. On the evening of the latter day there was some evacuation of flatus. On January 18, 1 c.c. pituitrin resulted in one fluid evacuation, and on January 19 there was incontinence of fluid fæces, which became frequent in the following days up to his death on January 25, from bronchopneumonia. Autopsy revealed complete section of the spinal cord at 10th dorsal level by crush fracture of 8th and 9th dorsal vertebræ.

Our investigation of this patient was made at the bedside on January 18, just before the first fluid motion, so that whatever effect may be related to distension by flatus had been in greater part relieved by pituitrin. Stimulation of the sole of the left foot induced slight contraction in the hamstring muscles of that side, but no other effect. Stimulation of the sole of the right foot evoked well-defined plantar flexion of the right great toe with a very slight contraction of the hamstring muscles. There was no anal reflex, and the knee and ankle jerks were lacking. Inflation of the rectal and anal balloons was made by air and syringe as usual and the pressure readings made by mercury manometer. The graph of resistance of the sphincter to gradual distension is shown in fig. 25, where its high resistance is readily observed. To digital palpation the sphincter felt very resistant, and though distension evoked an immediate plastic reaction the high tone was rapidly reasserted if the finger were kept still. Sudden distension of the rectal balloon with amounts up to 50 c.c. evoked a small relaxation of the sphincter (fig. 79) lasting forty seconds. This was not seen with increments of rectal volume below 50 c.c. The pressure within the rectal balloon revealed no contractile activity and was lacking in any plastic adaptation following a sudden distension. The rectum therefore appeared entirely inactive, the small effect of its passive stretch on the sphincter was the only evidence of co-ordinated effect.

We have already observed that the general lowering of postural tone of the sphincter ani is often but a reflection of some degree of activity of the rectum and probably distal colon, depending upon the degree of their distension. Thus in cases of cauda equina lesion the sphincter ani may be moderately resistant if the rectum has been emptied as in Case 1. The moderately high resistance of the sphincter ani in Case 12, during spinal shock, is therefore entirely attributable to inactivity of the rectum and colon. It is in fact the normal tone of the sphincter, fully developed. The direct effect of spinal shock on the postural mechanism

of the sphincter is therefore slight at this stage. From the very nature of the relaxing effect of distension of the rectum upon the internal sphincter ani the initial gaping of the sphincter following section of the pelvic nerves or sacral roots in animals is not evidence that the tone of the sphincter is dependent upon the integrity of these nerves, when the rectum may contain hard masses which it cannot dislodge. Still less does the pressure of fluid in the rectum sufficient to pass the sphincter [10] reflect the tone of the latter. Immediately following section of the sacral dorsal roots Merzbacher [25] found the anal sphincter contracted and only on the second day was it relaxed, while Garry [11] states that dilatation following section of the pelvic nerves in animals is "not a constant response." We have not had an opportunity of examining the sphincter in the first hours of spinal shock when the rectum was empty, but the parallelism between the tonic condition we found in Case 12 with that of the vesical sphincter under similar conditions is obvious. The postural mechanism particular to both vesical and rectal involuntary sphincters appears to be briefly if at all subject to spinal shock, and largely independent of the central nervous system. Relaxation of the vesical sphincter awaits the recovery of active contraction of the detrusor. That of the anal sphincter awaits recovery of rectal contraction, and is preserved from absolute closure only by the small relaxing effect of purely passive stretch of the rectal wall.

The effect of spinal shock on the rectum and colon is one of deep depression. We have presented evidence which strongly suggests that the function of automatic defæcation is integrated by the activity of the local nervous plexus. The depression of rectal and vesical function by spinal shock reflects the loss of that central nervous control which allows the correlation of reflex defæcation or micturition. The subsequent recovery of automatic local function is recovery from this depression. The segmental spinal reflexes in skeletal muscle, once recovered from spinal shock, are not affected by a further spinal transection at lower level. We are not aware of any observation on this point in the case of the bladder or rectum. Once reflex function is recovered in these organs, however, failure of the spinal reflexes of the isolated segment engenders a further period of "shock" in the peripheral nervous plexus concerned from which automatic micturition and defæcation emerge if the patient survives. There are here two levels of higher subsidy of reflexes, so to say, compared with one in skeletal reflexes. The permanent depression of automatic function following severance of the

afferent sacral roots (Merzbacher [25]) is more complex, and may provisionally be regarded as retention of the dominance of the ventral roots without afferent keys to unlock the chain of reflexes. States of persistent depression from partial lesions of the sensory tracts, as in tabes, or of the conus as in Case 11, appear to require this mode of explanation.

Spinal shock is essentially an affection of reflex nervous function; an extinction of reflexes by raised threshold of neuronal excitability. Its affection of the motor nervous mechanism serving micturition and defæcation is further evidence of the reflex nature of that peripheral function, albeit related to a peripheral ganglionic plexus of apparently identical histological structure to those sympathetic ganglia of known purity of efferent function. The local mechanism of both bladder and rectum appears closely to resemble that of the myenteric plexus.

The Sympathetic Nervous Pathway and the Participation of the Pelvic Colon.

The phenomena of automatic defæcation have striking contrast with those of automatic micturition, which in the normal subject very rapidly vanish when subjected to willed restraint [7]. Voluntary effort to suppress evacuation from either the bladder or the rectum is immediately effective owing to rapid and powerful closure of the external voluntary sphincters. The rectum, however, continues in contraction, and rhythmical waves have been observed to continue for one minute in spite of prolonged effort to overcome them. Vesical contraction, when extremely intense, is difficult to suppress by voluntary efforts, but even small spontaneous fluctuations in rectal pressure appear to be immune to voluntary inhibition. Relaxation of the effort at any stage reveals that the internal sphincter is still relaxed, so that it also is unaffected by the voluntary effort. The reaction of automatic defæcation declines in a manner so gradual as to be comparable to its defeat by mechanical obstruction. This finding confirms the surgical experience of abolition of voluntary control by surgical interruption of the external sphincter, though we do not agree with Matti [24] that the effect on the internal sphincter is other than that reflecting unbridled rectal activity.

Since voluntary control cannot thus be demonstrated in the reactions of the rectum and anal sphincter, it is perhaps superfluous to note that lesions of the cauda equina below the lumbar sympathetic outflow do not leave any willed effect on these organs referable to this pathway of innervation. Investigation of a case of surgical interference with this pathway was of interest, however, to determine the possibility of change

in the involuntary mechanism, particularly since it is stated that stimulation of the hypogastric nerves in animals has various effects on the colon, and contraction of the internal anal sphincter. We are indebted to Mr. Corbett, of St. Bartholomew's Hospital, for permission to investigate the following case under his care :—

Case 13.—Megacolon, operative resection of hypogastric nerves (presacral neurectomy).

T. A., male, aged 54, commenced to suffer from pains in the upper abdomen and from constipation five years earlier. Examination revealed stasis in the colon (megacolon). In July, 1934, the condition was verified by exploratory laparotomy and a cystocolic fold was divided, as well as an adhesion between the duodeno-jejunal flexure and the transverse colon. After an interval of freedom from pain, still subject to constipation, he suffered renewed pain in November, 1934, and it was then found that $4\frac{1}{2}$ pints of opaque fluid were necessary to fill the descending colon alone, and $6\frac{1}{2}$ pints to fill the entire colon. When the radiological appearance was watched under the influence of a spinal anæsthetic, the descending colon, and to less extent the remainder of the colon, were seen to begin to contract, returning the enema. Accordingly, on November 9, 1934, portions of the nerves around the inferior mesenteric artery and the adjacent area of aorta were resected at operation. The hypogastric nerves were readily defined, and their interruption beyond question. The patient remained still constipated, though satisfactory evacuation was secured by enemata.

Five weeks after operative resection of the hypogastric nerves our investigation revealed a lower degree of resistance to inflation of the rectum than normal, so that 60 c.c. was required to bring about the level of maintained contraction normally induced by 30 c.c. Small waves of contraction were observed at full inflation (fig. 78). The sphincter ani was normally resistant when inflated by gradual increments (fig. 24), and digital palpation also revealed no abnormality. Inflation of the rectal balloon from 40 to 60 c.c. induced a small phasic relaxation of the sphincter [provoked by inflation from 10 to 20 c.c. in the normal subject] (fig. 77). Distension of the intervening segment brought about a natural relaxation of the anal sphincter and rising, but low, rectal pressure, with a little evacuation in later stages. Stimulation of the sole of the foot induced a brisk contraction of the external anal sphincter. The behaviour of the sphincter and rectum was therefore of normal order, except for a change related to increase in rectal capacity and present before operation. We have ourselves no direct evidence as to this initial change responsible for the condition of megacolon, but in this patient the poverty of relaxing effect on the sphincter ani, even

with full distension of the rectum, is in full accord with the findings of Hurst [20] that here there is an achalasia, or affection of relaxation of the sphincter, by reason of damage to the local nervous plexus linking rectum and sphincter.

We found no change in tone of the sphincter and no absolute loss of the interaction between rectum and anal sphincter attributable to complete absence of hypogastric innervation, just as we find, in comparing Case 5 with Cases 6, 7 and 8, no change referable to the inclusion of the sympathetic innervation with the upper spinal segment in the latter cases. In both types of case distension of the upper rectum or colon with fluid varies the excitability of the lower rectum and lowers the tone of the sphincter ani, so that the reservoir organ as a whole has some reciprocal relationship with the sphincter. Learmonth and Rankin [21] have demonstrated that stimulation of the hypogastric (presacral) nerve in man brings about "strong clonic contraction of the sphincter, followed by several weaker clonic contractions." The type of contraction is evidently that peculiar to the sphincter ani and its provocation in this manner does not entitle the statement that "the thoracolumbar outflow provides the motor nerve supply for this muscle" [21] if by "the motor nerve supply" is meant any effect essential to the usual motor functions of the muscle. In the same manner the rectum appears to share the same independence of sympathetic function as is reported of the rest of the bowel [5].

Any hypothesis of lack of balance resulting from the overaction of the remaining pathway when one or other of the sympathetic or parasympathetic nerve supply of the rectum is interrupted is as unsatisfactory in explanation of clinical disorders of defæcation as we have found it in the parallel disturbances of micturition [8]. In the first place clinical disorder of these functions follows surgical interruption of only one of these pathways, the pelvic (sacral) nerve. Secondly, recovery of function following interruption of the pelvic nerve occurs in identical manner whether the remaining innervation be present or not. Sympathetic innervation appears as inessential to these organs as it is for the function of the heart or the salivary glands. We find full agreement with Cannon [5] that it is in emergency function that the sympathetic system has its value to the individual. Garry [12] has made the pertinent suggestion that where an inhibitory effect of section of the sympathetic nervous supply has been demonstrated by increased activity at open operation in animals the operative exposure has itself possibly supplied the state of emergency.

The question whether distant effects, such as the occasional participation of the whole colon in defæcation, as first described by Hurst [18, 19] and since observed by many others, is mediated by any central pathway is beyond the scope of the present investigation. There is no apparent defect in the delivery of fæcal material, either fluid or solid, to the rectum in the class of nervous disturbance we have investigated. McIntosh [22] has described a delay in the passage of a barium meal through the colon in a child suffering from an obscure lesion of the lumbro-sacral spinal cord. From the dilatation of the rectum and pelvic colon it would appear that here the effect of previous dyschezia has produced sufficient accumulation to retard the progress of the barium.

Our method of investigation has not been designed to give evidence of the behaviour of the region of the pelvi-rectal junction (O'Beirne's "sphincter" [29] or "superior rectal valve" of Houston, as defined by Paterson [31]). Although there is here often a change in the folding of the mucosa, both this and the common post-mortem anatomical narrowing suggestive of the presence of a sphincter are inconstant features (Paterson[31], Hurst[20], and Martin and Burden[23]) and there is no distinct change of the nature of the muscular layers. Hurst[20] states that he does not now believe that any sphincter exists at the pelvi-rectal flexure responsible for the radiological and anatomical appearance but considers it a kink produced by the mobility of the pelvic colon. He has observed [19] that colonic movement does not propel fæces beyond this region unless desire for defæcation is about to occur. We have observed that the further our rectal balloon was separated from the sphincter ani the less local contraction occurred in response to its distension and the less relaxation of the anal sphincter. Distension of the distal colon with fluid appears to have a general relaxing effect on the sphincter ani. A similar more phasic reaction has been noted in experiments upon animals, where Garry[11] describes a reflex dilatation of both the rectum and anal sphincter resulting from movement, but not distension, in the pelvic colon. We prefer to regard the pelvic colon as possessing the same motor function as the rectum, but in less degree. Small masses reaching the rectum are not returned to the colon if not excreted, but larger fluid or semi-fluid masses appear to us to be readily returned to the distal colon if defæcation is obstructed. It therefore appears possible that the most distal pelvic colon and the rectum together serve as an evacuating mechanism which, when filled in sufficient degree from above, contracts powerfully upon its contents and expresses them through the sphincter ani. If the external sphincter obstructs the

passage the same contraction drives the greater bulk to the reservoir of the distal colon. On this view the region of the pelvi-rectal junction has significance not as sphincter but as a region of transition from a canal reacting to the distension by its contents by rare massive contractions with long quiet intervals, to a canal reacting to increasing pressure by immediate and cumulative contraction. Our evidence relates only to fluids, however, and the retreat of solid fæcal material has no clear supporting observation. Although well-defined branches of the pelvic (sacral) nerve innervate the pelvic and descending colon [37, 26] the mechanism we have outlined has automatic function following impairment of this innervation, at least as far as the upper rectum. The effect observed by Garry[11] was accounted a reflex by him on account of its absence immediately following section of the pelvic nerves. We feel that a period of subsequent observation for its possible eventual recovery from the resulting depression would be desirable.

We have demonstrated that both following a transverse lesion of the spinal cord or cauda equina fully developed automatic defæcation can secure efficient evacuation of fluids, and that this reaction can be elicited from the rectum alone. The defective evacuation of solids resulting from these nervous lesions appears therefore to result not from deficient reaction to distension of the rectum but from lack of sufficient propulsive power in the act. The deficiency is not an absence of peristalsis, which is as little evident in contraction of the rectum in the normal subject as in these patients. It appears to be related to the general force of contraction of the rectum, which is far greater in the normal subject when evacuating both fluids and solids, even when the abdomen is purposely maintained relaxed. Hurst [19] attributes the lack of evacuation resulting from nervous lesions to lack of appropriate abdominal contraction owing to defective sense of rectal distension, and without doubt rises of abdominal pressure would stimulate the rectum and colon to earlier and more complete contraction. We would urge that the force of contraction of the rectum is the primary factor, without which evacuation, even of fluids, is impossible. When this contractile process is lacking, as in recent cauda equina or conus lesions, abdominal contraction is without effect, just as it is without effect in the inactive rectum of primary dyschezia of otherwise healthy people.

Varying degrees of dyschezia result therefore from the different stages of recovery of the local automatic and reflex mechanism of the rectum from the depression following isolation from the remainder of the nervous system. Even with the most complete recovery of these

functions efficiency is still lower than in the natural state, so that the familiar clinical picture of dyschezia with solid fæces and intermittent incontinence of liquid stools results.

Summary of Conclusions.

(1) Automatic defæcation resulting from destructive lesions of the sacral innervation of the rectum and anus in man has been studied. In it we have found contraction of the rectum with reciprocal relaxation of the anal sphincter.

(2) This reciprocal relationship between rectum and involuntary sphincter is nervous in mechanism. The adequate stimulus is tension upon the wall of the rectum. Passive tension appears sufficient to bring about slight relaxation of the sphincter. Active tension is a more powerful stimulus.

(3) The nervous mechanism for this "reflex" reaction appears to be related solely to the peripheral nervous plexus.

(4) The mechanism is subject to depression by spinal shock for a brief period during which the sphincter ani relaxes only slightly in response to passive distension of the rectum.

(5) Reflex activity of the sacral segments of the spinal cord brings a progressive character and greater fusion to the rectal contractions with consequent more massive and complete response ("reflex defæcation").

(6) Cutaneous stimulation in the skin area of the sacral segments, with maximal effect at the anus, and activity of the bladder, both facilitate the occurrence of reflex defæcation.

(7) The sympathetic nervous supply (hypogastric nerves) to the rectum and anus does not mediate these automatic and reflex responses.

(8) The postural tone of rectum and sphincter ani is a reaction to passive tension of the muscle concerned. In each a rapidly increasing tension causes tonic contraction to give way to phasic contraction, so that tension is also the stimulus for phasic movement.

(9) The mechanism of postural tone of the sphincter ani is local, and probably is related to the peripheral (? intramural) nervous plexus. It is essentially unaffected as a result of transverse spinal lesions, and the changes in the tonicity of the sphincter reflect only the degree of activity of the rectum and possibly the distal colon.

(10) Voluntary control over defæcation extends directly only to the external voluntary sphincter ani.

(11) The external sphincter is not tonic, though it contracts

reflexly in the course of the flexion reflex, and in synergy with the remainder of the abdominal parietes.

(12) The mechanism of defæcation, provided delivery of fæcal material from the colon is adequate, depends primarily upon the reaction of the rectum to distension.

(13) The inefficiency of defæcation resulting from transverse spinal lesions has explanation in the relatively small force of rectal contraction even with ample recovery of automatic or reflex function.

(14) The functions of micturition and defæcation are almost entirely comparable in their reaction to transverse lesions of the cord. Their mechanism is almost identical except for the lack of any potent voluntary inhibitory control over the contractions of the rectum.

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DESCRIPTION OF PLATES.

PLATE XII.

Graphic representation of the pressures within the recorder in the sphincter ani for each cubic centimetre of air introduced when distension was made 1 c.c. at a time at 8 second intervals. The pressure falls during each interval an amount represented by a vertical fall in the graph. The volume of air introduced is plotted in cubic centimetres on the abcissa, the resulting pressure in centimetres of water on the ordinates. The rise of tension resulting when the recorder is inflated in this manner outside the sphincter is shown in fig. 15 *b*. If the recorder were inflated with its centre 10 cm. below the surface of a bath of water the curve is parallel to fig. 15 *b* after the introduction of the first 1 c.c. and 10 cm. higher at each point. Fig. 12 is from Case 1. Figs. 13 *a* and *b* are from Case 2 under different circumstances (see text). Fig. 14 is from Case 3, and fig. 15 *a* from Case 4. Fig. 16 is from Case 5, and fig. 17 *a* and *b* from Case 6 under differing circumstances (see text). Fig. 18 is from Case 7. This recorder was not in use at the time Case 8 was investigated. Fig. 19 is from Case 9.

PLATE XIII.

Graphs obtained as in Plate XII. Fig. 20 is from Case 10. The data corresponding to the region of the broken line were not recorded as the pressures took the image beyond the edge of the recording paper (over 115 cm. water). Fig. 21 is from Case 11. Fig. 22 *a* and *b* are from a normal subject under different circumstances (see text). Fig. 23 is from another normal subject. Fig. 24 is from Case 13 (presacral neurectomy) and fig. 25 is from Case 12 (spinal shock).

PLATE XIV.

All this and subsequent Plates read from left to right. Time is shown by vertical strokes at 10 second intervals at the top of each record. R.P. indicates the pressure within the rectal balloon, S.P. indicates the tracing of pressure within the recorder in the sphincter, and the curve I.S. traces the pressure in the "intervening segment" where recorded. The tracing Abd. records the movement of the abdominal wall (downward for outward movement as in inspiration). The calibration for the rectal and sphincteric pressures is shown with the first record of each case.

Fig. 26.—From Case 1. The sphincteric recorder is inflated suddenly with 5 c.c. of air at *a*. The rectal balloon is suddenly inflated with 5 c.c. of air at *b*, with a further 5 c.c. at *d*, and a further 10 c.c. at *g*. From *l* to *m* 15 c.c. of fluid is run into the "intervening segment," so that the manometer (I.S.) thereafter records the pressure in this region.

Fig. 27. Also from Case 1, to show spontaneous fluctuations in pressure in the sphincter, the rectum not being inflated. At *a* brief passive pressure is applied to the abdomen. Recorder contains 6 c.c.

Fig. 28.—From Case 2. 50 c.c. air in rectal balloon. 10 c.c. air in sphincteric recorder. From *b* to *c* 25 c.c. fluid is run into intervening segment. From *d* to *e* an additional 100 c.c. is run in.

Fig. 29.—From Case 2 as fig. 28, except that at *a* and *e* the rectal balloon is completely deflated, at *b* and *f* suddenly inflated with 50 c.c. air. The rectal balloon is almost completely deflated at *h*, and at *i* and *j* 1 c.c. is rapidly introduced and immediately withdrawn. At *k* and *l* this is repeated with 5 c.c. and from *m* to *o* 5 c.c. are repeatedly introduced and withdrawn in rapid succession, and finally left in.

FIG. 30.—From Case 2, as figs. 28 and 29. At *a* 50 c.c. air is introduced into the rectum. The whole perineum was observed to relax (see text), the density of the small vertical markings record the approximate degree of relaxation of the perineum as observed by eye. The patient moved slightly at *b*. At *c* the rectal balloon was deflated, and at ↑ at *d* was withdrawn 10 cm. until its attachment lay just above the sphincter recorder. At *e* it was reinflated with 50 c.c. air.

FIG. 31.—From Case 3. The sphincter recorder contains 15 c.c. air, the rectal balloon 10 c.c. air. At *a* 40 c.c. air is injected into the rectal balloon.

FIG. 32.—Case 3. The rectal balloon contains 40 c.c., the sphincter recorder 10 c.c. Between *a* and *b* 50 c.c. of fluid is run into the intervening segment. Evacuation past the sphincter occurs in the duration of the thick horizontal line.

FIG. 33.—Forty seconds after fig. 32. Between *a* and *b* 300 c.c. of fluid is allowed to enter the intervening segment. Evacuation is shown by the thick lower horizontal line.

FIG. 34.—As fig. 33. At ↑ spontaneous micturition was observed to commence, and ceased at ↓. Evacuation of fluid past the sphincter ani occurred in the period shown by the duration of the thick horizontal line (EVAC).

PLATE XV.

FIG. 35.—Case 5. The sphincteric recorder contains 10 c.c. air. At *a* the volume of the rectal balloon is suddenly increased from 10 c.c. air to 40 c.c. air.

FIG. 36.—Case 5. The rectal balloon contains 30 c.c. air, the sphincter recorder 4 c.c. Between *a* and *b* 100 c.c. fluid is run into the intervening segment.

FIG. 37.—Case 5. The rectal balloon contains 40 c.c., the sphincter recorder 4 c.c., and the intervening segment 50 c.c. At *a* the sole of the right foot is scratched. Evacuation of semi-solid fæcal material occurs in the duration of the horizontal lines (EVAC), and tends to extrude the recorders.

FIG. 38.—Case 5, as fig. 37. At *a* the sphincter recorder is suddenly distended with a further 4 c.c. air. Evacuation commences as shown and continues.

FIG. 39.—Case 6. 6 c.c. air in sphincter recorder. At *a* 30 c.c. air is injected into the rectal balloon.

FIG. 40.—Case 6. 10 c.c. air in sphincter recorder, 40 c.c. in rectal balloon. At *a*, *b* and *c* scratches were made in the skin at the right side of the anus.

FIG. 41.—Case 6. 50 c.c. air in rectal balloon, 10 c.c. in sphincter recorder. In the duration of the horizontal line at *a*, the recorder was rotated in the sphincter through some 20 to 30 degrees.

FIG. 42.—As fig. 41. At *a* the recorder was moved quickly outwards in the sphincter and then held still.

FIG. 43.—Case 7. Effect of injection of 25 c.c. air into the rectal balloon. The sphincter recorder was here a small balloon without central core, so that rectal pressure is recorded by it in some degree.

FIG. 44.—Case 7. Rectal balloon contains about 40 c.c. Sphincteric recorder, without core, moderately distended. Between *a* and *b* 100 c.c. fluid run into intervening segment. No evacuation.

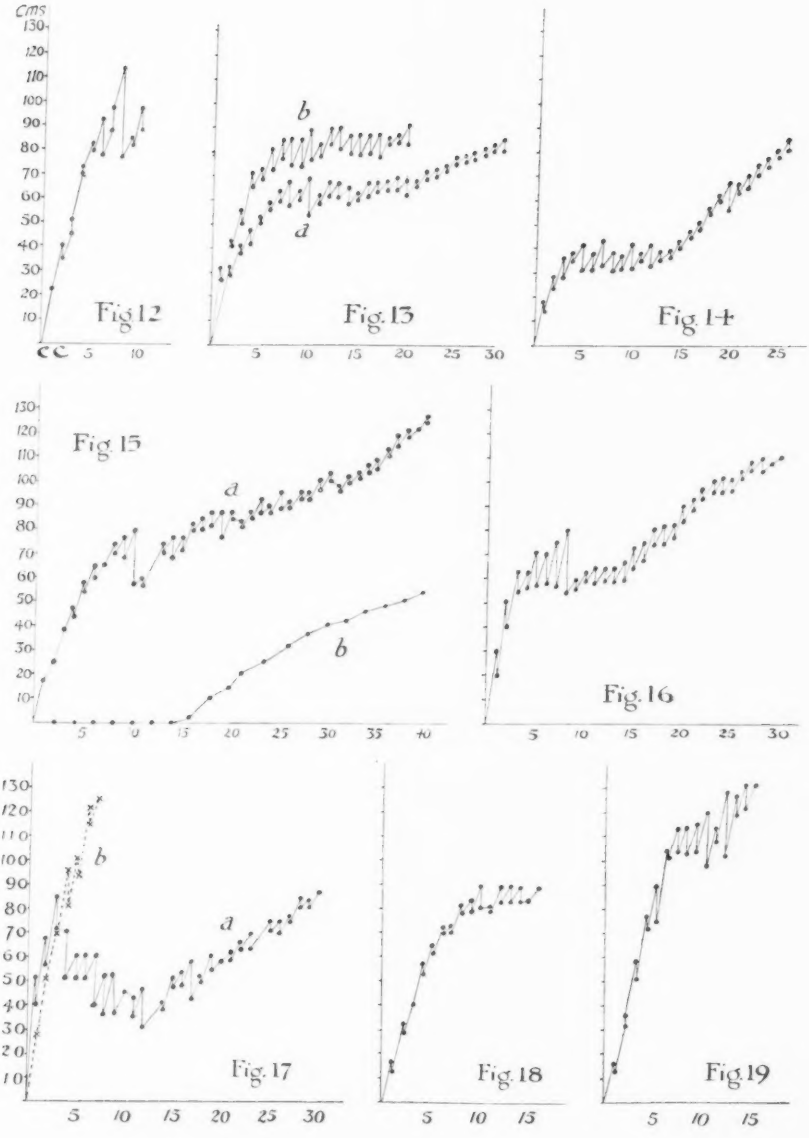
FIG. 45.—Case 7. Rectal balloon contains 50 c.c. Intervening segment slightly distended. Sphincter recorder moderately distended (with fresh pressure scale). At ↑ the bladder was gradually distended until micturition occurred in the duration of the horizontal line at M. No evacuation from rectum.

FIG. 46.—Case 7. Tensions as fig. 43. 50 c.c. air in rectal balloon. Sphincter moderately distended. Spontaneous waves.

FIG. 47.—Case 7. As fig. 43. In addition to the record of rectal pressure (R.P.) and pressure within the anal sphincter (S.P.) and intervening segment (I.S.) there is also recorded vesical pressure (V.P.). At ↑ the fluid commences to distend the bladder, and at ↓ the inflow is shut off. The resulting micturition occurs in the duration of the double line M, and evacuation from the rectum occurs in the period shown by the thick line (EVAC).

FIG. 48.—As fig. 47. The bladder is partly distended (50 c.c.). A sharp spike, *a*, shows where a brief passive pressure is made upon the abdominal wall.

PLATE XII.



To illustrate paper by D. Denny-Brown and E. Graeme Robertson.

PLATE XIII.

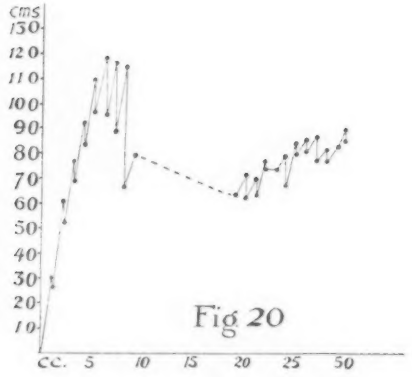


Fig 20

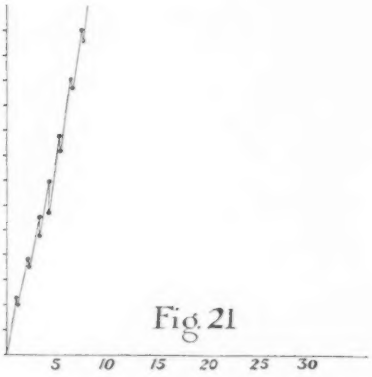


Fig. 21

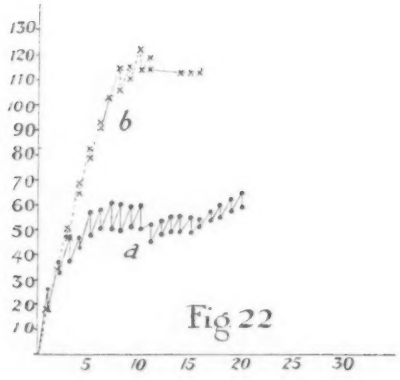


Fig 22

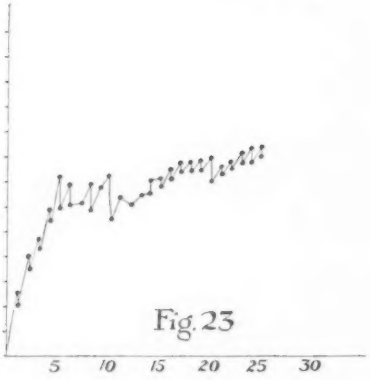


Fig. 23

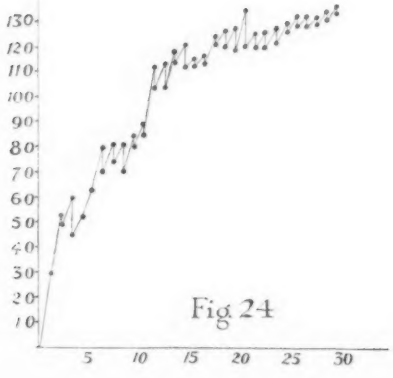


Fig 24

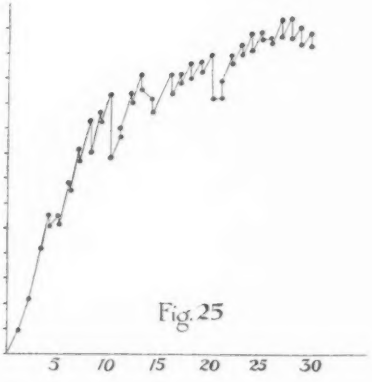
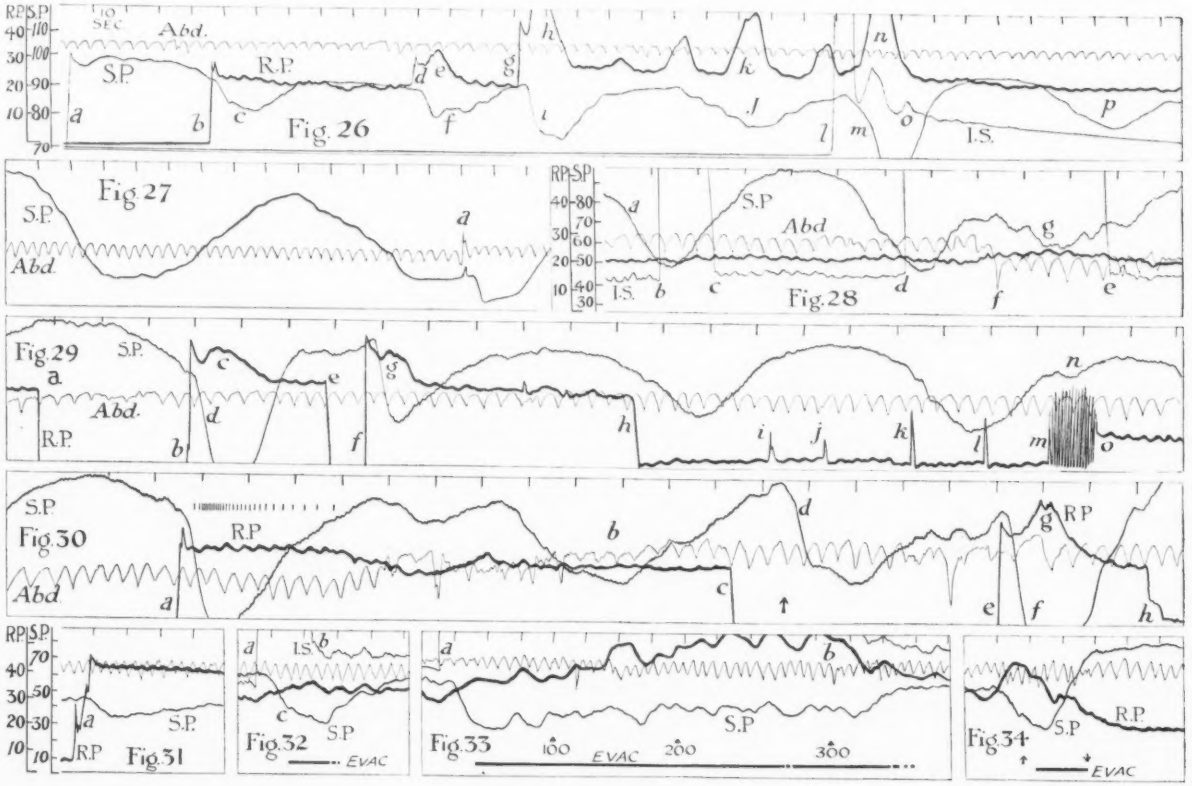
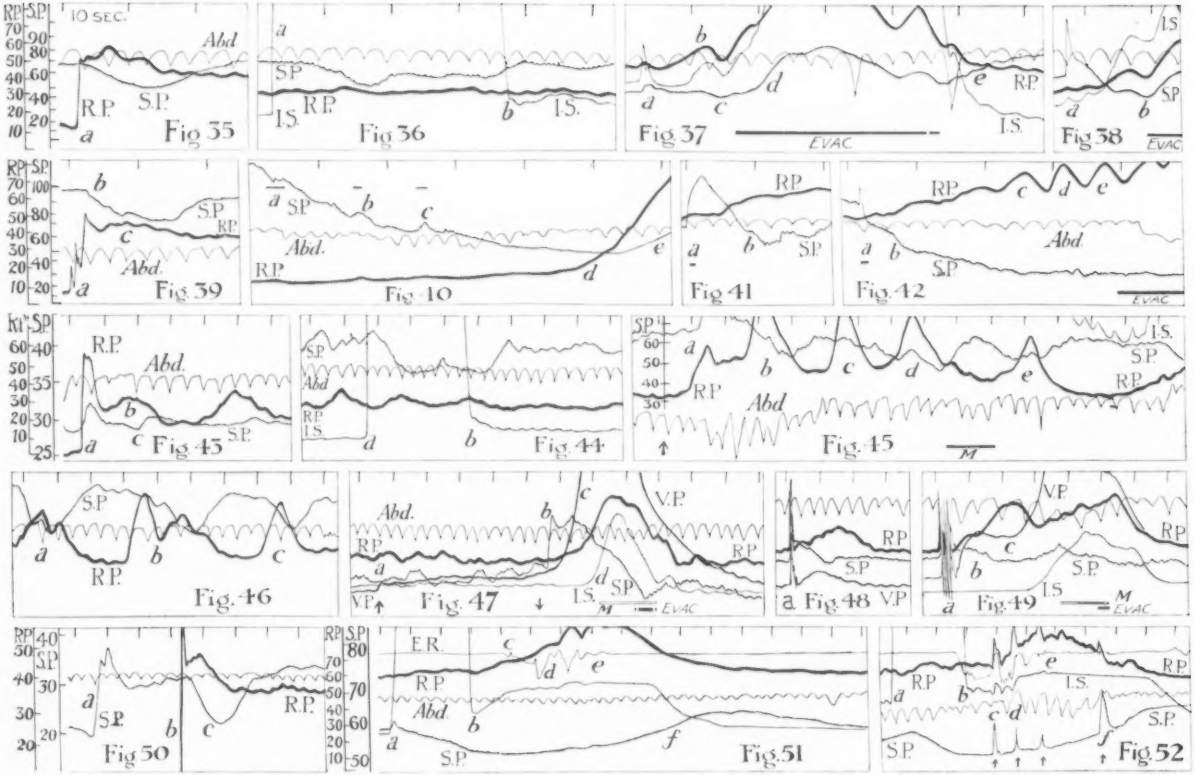


Fig. 25

To illustrate paper by D. Denny-Brown and E. Graeme Robertson.

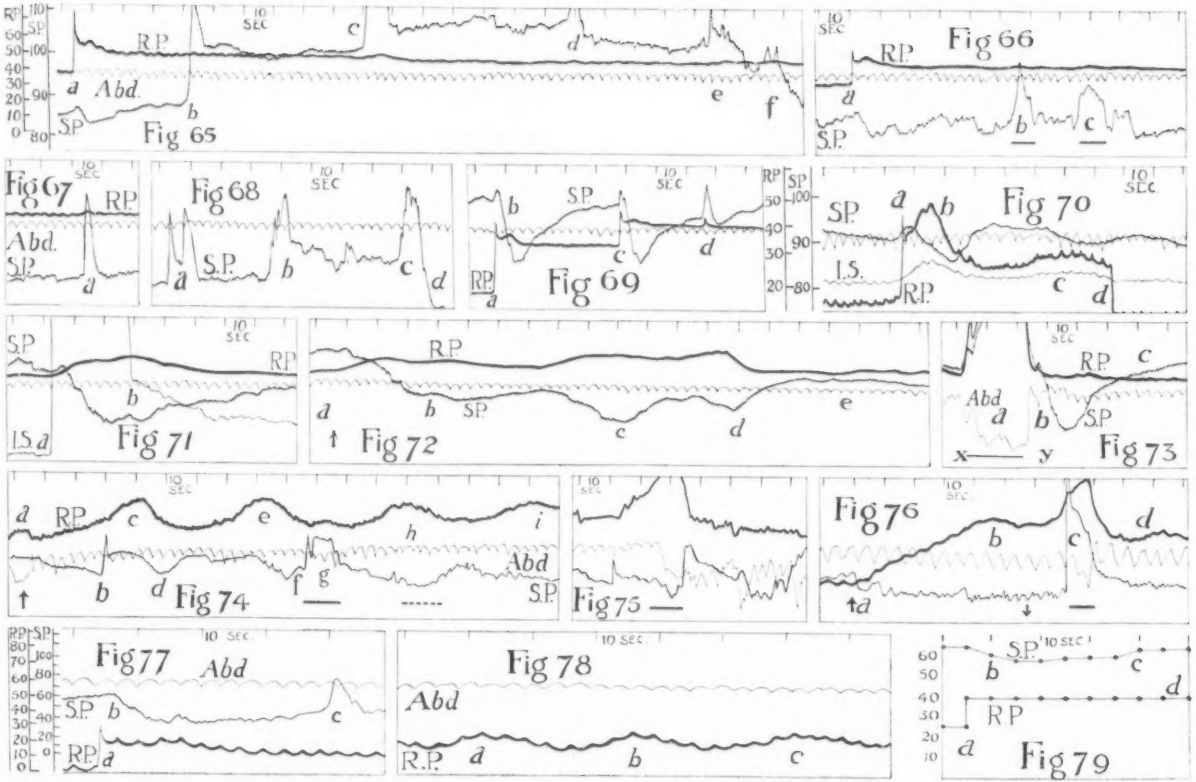


To illustrate paper by D. Denny-Brown and E. Graeme Robertson.



To illustrate paper by D. Denny-Brown and E. Graeme Robertson.

To illustrate paper by D. Denny-Brown and E. Graeme Robertson.



To illustrate paper by D. Denny-Brown and E. Greene Robertson.

FIG. 49.—As fig. 47. Effect of repeated passive abdominal pressure at *a*.

FIG. 50.—Case 8. Small coreless balloon used to record pressure in sphincter ani. This was fully distended at *a*. The rectal balloon was distended suddenly with 30 c.c. air at *b*.

FIG. 51.—Case 8. Rectal balloon contained 40 c.c. air. Small coreless balloon in sphincter ani fully distended. Funnel at anus records evacuation of fluid (*c*, *d*, *e*) by downward deflection of tracing, E.R. 50 c.c. fluid is run into the intervening segment between *a* and *b*.

FIG. 52.—Case 8. As fig. 51, except that at the points marked ↑ ↑ ↑ ↑ the outer border of the sole of the right foot was scratched, with resulting brief closure of the sphincter.

PLATE XVI.

FIG. 53.—From Case 8. Rectal balloon contains 30 c.c., sphincteric recorder contains 3 c.c. At *a* a sudden brief passive pressure upon the abdomen elicits a brief contraction of the sphincter followed by a relaxation associated with a wave of rectal contraction, *b*. At *c* a scratch on the inner sole of the left foot elicits a brief contraction of the external sphincter with similar relaxation of the internal sphincter and rectal contraction at *d*.

FIG. 54.—Case 8. As fig. 53. Rectal balloon contains 40 c.c. air, 3 c.c. in balloon in sphincter. In the period shown by a black horizontal line the rectal balloon was pulled gently downwards. A prolonged powerful contraction of the rectum was set up.

FIG. 55.—Case 8. As fig 54. At *a*, and again at *b*, the sphincter recorder was twisted very slightly.

FIG. 56.—Case 9. Rectal balloon contains 20 c.c. Recorder in sphincter 7 c.c. At *a* is seen one of the regular spontaneous fluctuations in pressure in the sphincter. At *b* the rectal balloon is suddenly deflated. At *c* it is suddenly inflated with 20 c.c. air. There is a slight relaxation of the sphincter from *d* to *e*. The rectal balloon is then again deflated.

FIG. 57.—Case 9. As fig. 56. The rectal balloon contains 20 c.c. Fluid was being run gradually into the "intervening segment" and at the commencement of the record 300 c.c. had entered. Between 450 and 500 c.c. the inflow was shut off for twenty seconds, and was then continuous to 850 c.c. when it was shut off (*k*). The sole of the foot was scratched at *i*.

FIG. 58.—Case 10. The rectal balloon contains 30 c.c. air. At *a* an additional 20 c.c. is suddenly added. The wave *b* is due to rectal contraction. At *c* a large wave of rectal contraction occurs in response to digital exploration of the sphincter.

FIG. 59.—Case 10. The rectal balloon contains 50 c.c. air. The sphincter recorder had been slowly distended with 30 c.c. air. At *a* the whole perineum was observed to withdraw spontaneously in the period of high pressure in the sphincter. No evacuation occurred.

FIG. 60.—Case 10. Rectal balloon contains 30 c.c. At *a* the recorder in the sphincter, which contained 2 c.c. air, was suddenly inflated with an additional 8 c.c. At *b* fluid was run into the intervening segment, reaching 50 c.c. at the end of the figure.

FIG. 61.—Case 10. As fig 60. At *a* the inflow of the intervening segment is opened and fluid run in continuously to the end of the figure. Evacuation of fluid past the sphincter occurred in the duration of the thick horizontal lines (EVAC).

FIG. 62.—Case 10. 40 c.c. in rectal balloon. 10 c.c. in sphincter recorder. 100 c.c. fluid in intervening segment. At *a* the patient coughed, at *b* two brief passive pressures on the abdomen. At *c* the perineum was observed to retract suddenly and relax slowly, and again at *e*. Slight evacuation of fluid at end.

FIG. 63.—Case 11. Sphincter recorder contains 4 c.c. Rectal balloon contains 30 c.c. air. At *a* an additional 10 c.c. is suddenly added to the rectal balloon and at *d* an additional 10 c.c. Rectal balloon deflated at *g*. The relaxations of the sphincter at *c* and at *f* are those occurring spontaneously at regular intervals as in fig. 64.

FIG. 64.—Case 11. 40 c.c. air in rectal balloon. 4 c.c. in sphincter recorder. At *a* a spontaneous relaxation of the sphincter briefly interrupted by efforts to contract the perineum voluntarily at *b* and at *c*. At *c* fluid is allowed to distend the intervening segment until 450 c.c. has entered (at *l*). There was no evacuation. At *m* the patient coughed, and at *n* the abdomen was subjected to a series of rapidly repeated pressures.

PLATE XVII.

FIG. 65.—Normal subject. Rectal balloon contains 30 c.c. air, sphincter recorder 10 c.c At *a* an additional 10 c.c. air introduced into rectum. The base of the sphincter recorder was not visible. At *b* the sphincter recorder was withdrawn about 1 cm. At *c*, *d*, *e* and *f* it was withdrawn 1 cm. in each step.

FIG. 66.—Normal subject. Rectal balloon contains 30 c.c. air, sphincter recorder contains 10 c.c. air and is in outer part of sphincter. At *a* an additional 10 c.c. is added to the rectal balloon. At *b* the subject, lying on the left side, extended the right lower limb. At *c* the limb was again flexed.

FIG. 67.—Continuation of fig. 66. At *a* the subject made a brief voluntary contraction of the perineum as if to restrain flatus.

FIG. 68.—Normal subject. As fig. 65. At *a* a brief voluntary restraint. At *b* the sphincter recorder is rapidly moved inwards 2 cm., and again at *c*, passing into the rectum at *d*.

FIG. 69.—Normal subject. Sphincter recorder contains 10 c.c. air and is held in relation to innermost portion of sphincter. At *a* the rectal balloon is suddenly inflated with 30 c.c. air, and at *c* with an additional 10 c.c. At *d* the subject coughed.

FIG. 70.—Normal subject. Sphincter recorder contains 4 c.c. and is related to both parts of the sphincter. At *a* 30 c.c. air is suddenly introduced into the rectal balloon and withdrawn at *d*.

FIG. 71.—Normal subject. 40 c.c. air in rectal balloon, 4 c.c. in sphincter recorder. From *a* to *b* 50 c.c. fluid is run into intervening segment. Tension scale of this figure and also figs. 72 and 73 as in fig. 65.

FIG. 72.—Normal subject. As fig. 71. At ↑ fluid commences to run continuously into the intervening segment until after the end of the figure.

FIG. 73.—One minute after end of fig. 72. In the period *x* to *y* the subject strained ineffectually in attempting to defæcate.

FIG. 74.—Normal subject. Tensions as fig. 70. Rectal balloon contains 40 c.c., sphincter recorder 4 c.c. Fluid is run into the intervening segment from ↑ to end of figure. At *g* the subject attempted to restrain voluntarily for the period of the horizontal line. Some sense of desire for defæcation felt in the period marked by a broken line at *h*.

FIG. 75.—Normal subject. As fig. 74. After long continuing distension of the intervening segment, one of the larger waves of rectal contraction evacuates a large quantity of fluid past the sphincter recorder in the period shown by the horizontal line. The subject then restrained voluntarily, but the rectum was already empty.

FIG. 76.—Normal subject. The rectal balloon contains 40 c.c. At ↑ fluid is run into the intervening segment until the point marked ↓. In the duration of the horizontal line at *c* the subject makes an effort of voluntary restraint.

FIG. 77.—Case 13. Rectal balloon contains 20 c.c. air, sphincter recorder 5 c.c. At *a* an additional 20 c.c. air is added suddenly to the rectal balloon. At *c* the patient involuntarily contracted the perineum.

FIG. 78.—Case 13. Slow rhythmic waves of contraction recorded by the rectal balloon when distended with 40 c.c. air.

FIG. 79.—Case 12. Chart of observed pressures in rectum and sphincter from observations at 5 second intervals at the bedside. Sphincter recorder contained 10 c.c. air. The rectal balloon contained 50 c.c. air, and at *a* an additional 10 c.c. was suddenly added.

A NOTE ON THE DEFINITION OF THE "MOTOR" AND "PREMOTOR" AREAS.

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F. M. R. WALSHE, in a critical survey [18] of a series of papers on the functions of the frontal lobes, recently published from this laboratory, has drawn attention to the fact that in arbitrarily limiting the term "motor area" to the area giganto-pyramidalis of the precentral convolution we have not properly heeded certain earlier neurological teachings, especially those of Hughlings Jackson. His treatment of our work would require no further comment were it not likely seriously to mislead those not intimately acquainted with the field.

I.

Since 1870 [7] the term "motor area" has been used both in neurological and experimental literature as synonymous with the electrically excitable area of the frontal lobes exclusive of the eye field. The work of Campbell [3], Brodmann [1] and others demonstrated in primates that the precentral excitable region was made up of two principal cyto-architectural areas, both evidently motor in function, and designated Area 6 and Area 4 respectively. The term "premotor area" has been introduced within the last ten years to designate the anterior part of the excitable area, but the new term has been used loosely and it has appeared essential to define it more precisely. The simplest and most obvious expedient, as the Vogts [17] and Foerster [5, 6, 7] have frequently pointed out, is to use a terminology that conforms to the principal cyto-architectural fields. After careful consideration of the matter and discussion with investigators in this country and in Europe, we decided a year ago[1] for the purpose of our laboratory publications

[1] Walshe is quite correct in stating that in some of our earlier papers terms were not adequately defined, and it was our own realization of the fact that caused us to adopt the newer usages [9]. We do not wish to imply that all the corticospinal tracts arise from the motor area, for many writers, most recently Kennard [15] and E. C. Hoff [12], have found that Area 6a contributes extensively to the corticospinal system, and that the terminal distribution in the cord of these corticospinal fibres differs from the distribution of those from Area 4 [12], which further substantiates the belief that these areas are functionally discrete.

to restrict the term "premotor area" to the cyto-architectural field designated "Area 6a" (upper part) as outlined by the Vogts and Foerster (see fig. 1). "Area 4" remained for designation, and it seemed entirely appropriate to restrict the term "motor area" to the field of the Betz cells, as had originally been done by Campbell [3] in 1905, and later by von Economo [4, p. 34]. This leaves the useful and non-committal phrase "the excitable area" as a comprehensive term applicable to both regions. The justification for this terminology lies in the fact that cyto-architectural definition has been found useful,

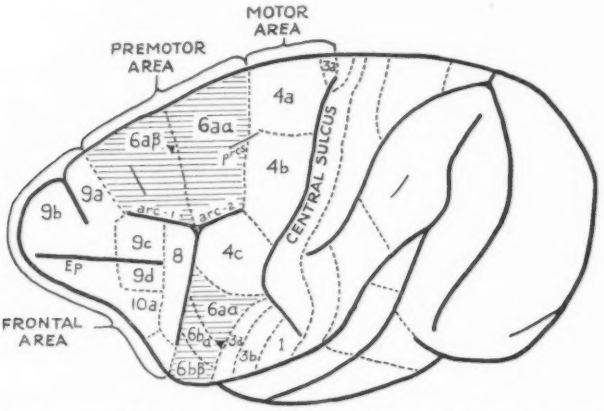

FIG. 1.—The cyto-architectural subdivisions of the frontal lobes of a cercopitheque monkey according to the Vogts [17]. This has formed the basis of Foerster and Penfield's map of the human cortex in which corresponding areas have been identified, and of Fulton and Kennard's studies of the chimpanzee cortex. The excitable cortex includes areas 4, 6 and 8 with their various subdivisions. The motor area is synonymous with area 4, the premotor with area 6a β and 6a α (upper part); areas 6a α (lower part), 6b α and 6b β have not received special designation. The eye field occupies area 8, and the frontal association region areas 9, 10, 11 and 12. Areas 11 and 12, which are on the orbital surface, are not shown on the figure.

and, indeed, indispensable, in considering other areas of discrete function in the cortex. If it is not in harmony with Hughlings Jackson's terminology (whose fundamental conceptions of levels of function are entirely consistent with the subdivision which we have urged), it is scarcely surprising since studies of cyto-architecture had not yet been undertaken in Jackson's time.

II.

Lest any further confusion arise, it is desirable briefly to summarise the observations (on chimpanzees) which Walshe has attempted to elucidate.

(1) *Area* 4.—Complete experimental ablation of Area 4 ("motor area" in our terminology) causes transient paralysis, most marked and enduring in the distal joints, transient depression of reflexes and transient flaccidity. In the stages of recovery from a lesion of Area 4 deep reflexes may become moderately hyperactive, but gross spasticity has never been observed at any age of recovery following lesions sharply restricted to area 4.[1]

(2) *Area* 6a.—Ablation of Area 6a (upper part, "premotor area" of our terminology) at a primary operation, or after removal of Area 4, causes a disorganisation of the more highly integrated voluntary movements [14] producing a state akin to apraxia in man (a term scarcely applicable to animals); and such lesions lead also to the immediate appearance of spasticity with increase of deep reflexes, forced grasping, vasomotor disturbances and certain specific reflex signs such as those of Rossolimo, Mendel-Bechterew, Hoffmann, and the fanning sign of Babinski [16].

(3) *Bilateral ablation of Area* 4 *and* 6a.—Bilateral ablations of motor and premotor areas in mature monkeys causes permanent paralysis of voluntary movements, and the postural reflex state of the skeletal musculature of such a preparation is indistinguishable from that of a thalamic monkey; but if a part of one area, motor or premotor, remains intact in one hemisphere, the animal recovers some degree of voluntary power in all four extremities.

(4) *Areas* 9, 10, 11 *and* 12.—Bilateral ablation of the frontal association areas does not cause forced grasping and gives rise to no other disturbance in reflexes or in motor skill; complex behavioural deficits appear, however, which are beyond the scope of this note and are fully described elsewhere [13, 14, 9, 11].

Walshe's discussion focusses attention upon the possible functional subdivisions of the premotor area, a problem which has been under investigation for several years, but we are not yet in a position to discuss the matter in detail beyond stating that the posterior half (Area 6a α of the Vogts, fig. 1) is more excitable than the anterior part (Area 6a β), and on stimulation yields more discrete movements (Vogts [17], Foerster and Penfield [5, 6], Bucy [2]), and that subtotal extirpation of the premotor area fails to produce forced grasping, i.e. removal of Area

[1] Prior to December 1932, we were unaware of the relation of Area 6a to spasticity and most of our early extirpations of Area 4 encroached upon the posterior part of Area 6a. This accounts for the transient spasticity with "Area 4" lesions in chimpanzees reported by Fulton and Keller [10] in June, 1932, and by Jacobsen [13].

6a α alone or Area 6a β alone does not give rise to the full premotor syndrome, whereas complete removal, even if carried out seriatim, causes it.

Walshe states that the sequence of cortical ablation was so rapid in some experiments that the motor status in the affected limbs did not reach equilibrium before it was further modified by a second lesion. This was true in experiments in which the state of equilibrium was not the object of our study, but lest misconception arise from this criticism it should be pointed out that the survivals in our ablation studies are the longest on record. A number of our chimpanzees have been under observation for periods ranging from one to three years following a single operation; one animal was observed and trained for two years before surgical procedure was instituted, and was studied for a year after an Area 4 ablation (during which a state of paresis, markedly flaccid at first, persisted in the affected extremity). When the premotor area was removed the previously flaccid extremity became highly spastic, and has remained spastic for a period of two and a half years. The animal is still alive after a sojourn of five years in the laboratory; and it has been examined by every clinical neurologist who has honoured our laboratory with a visit. The specific reflexes of Rossolimo and Mendel-Bechterew, and the fanning sign of Babinski, also have persisted throughout this two-and-a-half year period. A full summary of our work on the frontal lobe which formed the basis of a series of Herter lectures will presently be published.

It would be unbecoming further to take issue with Walshe because his "motor area" includes our "motor and premotor areas"; and when he states that lesions of his "motor area" give rise to all the symptoms which we have relegated to the syndrome of the "premotor area" he is of course entirely correct, except that he omits "forced grasping," which, on wholly insufficient evidence, he vaguely attributes to disturbances in some other part of the frontal lobes. Such differences, therefore, as exist between us are primarily those of definition.

Summary.

Since the anterior boundary of the excitable precentral cortex cannot be accurately defined in anatomical terms, and since the functions of the anterior part of the excitable cortex obviously differ from those of the posterior, a more precise terminology is needed to designate these functionally discrete regions. The term "premotor area" has been used in the past synonymously with the "intermediate precentral"

region, but adequate anatomical definition has not hitherto been given. Since these regions correspond roughly with well-recognized cyto-architectural fields, it is suggested that the following conventions be adopted (fig. 1). That:—

(1) *Motor area* be restricted to the area giganto-pyramidalis, i.e. Area 4 of Brodmann, the Vogts and Foerster.

(2) *Premotor area*, which is also motor in function, include Area 6a (upper part) of the Vogts, the posterior part being designated 6a α and the anterior part 6a β.

(3) *Frontal association areas* include Areas 9, 10, 11 and 12 of Brodmann.

The term "excitable area" is applicable to both the motor and premotor regions.

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Notices of Recent Publications.

The Carotid Sinus and the Cerebral Circulation. By Erik Ask-Upmark. *Acta Psychiatrica et Neurologica.* Supplement VI. Copenhagen: Levin and Muskgaard. 1935. Pp. 374.

Ask-Upmark has studied the anatomical relationships of the carotid sinus in animals; he observed the effect of sinus stimulation on pial vessels, and analysed the blood-pressure records of 486 of Cushing's cases of cerebral tumour. The work indicates great industry and painstaking effort, but the size of the volume seems out of proportion to the new material it contains.

The most substantial contribution is the report of dissections of the sinus region in twenty-seven different species of animals. Evidence of a sinus (though unfortunately histological confirmation could not be carried out) was present in all. It lies on the occipital artery if the carotid is lacking, and is intimately associated with the glossopharyngeal nerve. In an effort to establish a relationship between the sinus and the vasomotor nerves of the brain, Ask-Upmark watched the pial vessels of the cat during stimulation. Vasoconstriction, though usual, was the passive response to a fall of systemic blood-pressure. Active dilatation, if present, was relatively unimportant.

The author's effort to prove arterial hypotension in patients with cerebral tumour and to link it with invasion of the hypothalamus and hypophysis forms the body of the section on clinical aspects of the problem. He found that the cerebral vascular changes are in the main secondary to systemic changes, but he fails to make a fair-minded review of the prior work of Weiss and Baker, who have made a detailed investigation of the heart and circulation in a considerable group of these patients. He dismisses too lightly their demonstration that some who lose consciousness and have convulsive movements on pressure of the sinus, do not have coincident decrease of pulse, of blood-pressure or of cerebral blood flow. In these persons there must be neurological mechanisms at work which are not dependent on circulatory changes. This contribution of Ask-Upmark's, serious and detailed though it is, can be considered as an introduction, not as a conclusion, to the subject of the carotid sinus in man.

Thérapeutique Médicale: Système nerveux. Par M. Loeper, &c. Paris: Masson et Cie. 1935. Pp. 380. Price 50 fr.

This is the eighth volume of a system of therapeutics which has been edited by Professor Loeper. In its production he has obtained the collaboration of many well known neurologists and he consequently presents a review of French practice which must be interesting and instructive to English readers.

The first part, written by the Editor, deals with general principles, as the use of sedatives, hypnotics, analgesics and tonics. His presentation of these subjects is particularly valuable as he discusses the physiological and pharmacological actions of the drugs and other agents which he employs. The following chapters deal with the treatment of various diseases and pathological conditions as apoplexy, epilepsy, nervous syphilis, meningitis, migraine, &c., and with the use of fever therapy, radiotherapy in cerebral tumours, psychotherapy and the value of climate, baths and physical methods. Most of these chapters attain a high standard and are obviously written for the practitioner. Unfortunately the book lacks an index which would have added considerably to its value.

Les Nécroses Tachycardiques. Par L. GALLAVARDIN et A. TOURNIAIRE. Paris: Masson et Cie. 1935. Pp. 121. Price 17 fr.

This small monograph deals with the nature and the symptoms of nervous tachycardia or irritable heart as observed in military and civil practice. The various disturbances of function associated with the rapidity of the pulse are fully described and analysed, and the conclusion is reached that all of them can be attributed to abnormal excitability of the cardiac sympathetic fibres. The many interesting observations recorded and the objective treatment of the subject make the book worthy of careful study.

Les Ramollissements Protubérantiels. Par J. O. TRELLES. Paris: G. Doin et Cie. 1935. Pp. 306. Price 50 fr.

A monograph on the common and variable groups of symptoms associated with softening of the pons Varoli is timely, for though so frequently met with in clinical practice and often studied from the anatomical point of view, there has been no recent attempt to deal comprehensively with the subject or to correlate accurately the disturbances of function with the sites of the lesions responsible for them. This the author has done by the study of a large number of personally observed cases and a survey of many collected from the literature.

As the position and the extent of the lesion depends on the distribution of the vessel which is occluded he naturally starts with the vascular supply of the pons; a fuller description of this would have been acceptable, that which he gives is very schematic. The symptoms are grouped into syndromes each of which is determined by the anatomical distribution of the artery which is blocked: this facilitates description, but it is obvious that even in this compact and highly organized portion of the nervous system many cases refuse to fall into any such rigid classification. This does not, however, invalidate the clinical and anatomical observations which are published. One of the most interesting symptoms occasionally associated with lesions of the brain-stem, the so-called "palatal nystagmus," is discussed at length, and the author concludes that it is directly due to a special form of change in the bulbar

olives—the so-called "olivary hypertrophy"—which is usually secondary to interruption of the central tegmental tract or of other fibres related to the olives.

Volume Jubilaire en l'honneur du Professor Dr. C. I. Parhon. Jassy: Brawo. 1934. Pp. 555.

In celebration of the 60th birthday of their eminent colleague, the Roumanian Society of Neurology, Psychiatry, Psychology and Endocrinology have published this volume of 55 papers on subjects in which Professor Parhon is interested. Only a small number are devoted to neurological subjects, but some of these, as that on compression of the cord by tumours, are valuable contributions. Others deal with psychiatric and criminological problems and with the functions and disturbances of the endocrine organs. The volume is a fitting compliment to a distinguished neurologist whose activities have been characterized by the generous scope of his interests.

Nouveau Traité de Psychologie. Par GEORGES DUMAS. Tome Quatrième. Les Fonctions et les Lois Générales. Paris: Librairie Félix Alcan. 1934. Pp. 528.

This rather tardy but welcome volume of the series is in two parts, of which the first deals with the general organizing functions of the mind and the second with the general laws of mental activity. In spite of the somewhat unprecise nature of these topics the treatment is neither diffuse nor obscure. Professor Piéron is the author of the first two chapters, dealing with attention and memory, together with habit; he presents the matter in a critical, undogmatic and matter-of-fact way. After Henri Delacroix's brief paper on the association of ideas, in which the Freudian contribution to this subject receives unduly meagre notice, there is a more abstruse chapter on Schematization by Revault d'Allonnes. Professor Georges Dumas then presents what is rather an essay on Symbolism than a scientific exposition; there is much discussion of symbols as used in ordinary language and literature, especially French, and in religion. Professor Dumas is very cautious in his views and scarcely mentions the more audacious theories as to the rôle of symbols in mental life. Professor Blondel writes a valuable but somewhat sceptical exposition of the notions of synthesis and automatism which have played so conspicuous a part in French psychology. Pierre Janet briefly reviews the normal and pathological facts which can be brought together under the conception of psychic tension and its oscillations. Professor Poyer's contribution deals with the difficult but very important subject of fatigue and intellectual work; it is incomplete in its survey of the relevant literature but covers most of the significant matters. The last chapter, on sleep and waking, is in the expert hands of Professor Claparède: it is a striking example of the spirit that appears in all the contributions to this work, in that it gives a balanced, critical account of what has been discovered, together with a full statement of the gaps and problems that remain.

Schizophrenia : Statistical Studies from the Boston Psychopathic Hospital, 1925-1934. Published by the Massachusetts Society for Mental Hygiene and the Boston Psychopathic Hospital. 1935.

Psychiatry is still in the stage at which statistical checks upon clinical belief and research are essential. In the eighteen papers here reprinted, a patient attempt has been made to study various aspects of schizophrenia and other conditions by the application of strict statistical methods to the data collected by psychiatrists and social workers. Professor Edwin B. Wilson, of Harvard, who directed the statistical work, points out in his foreword how trifling and even misleading in its apparent results may be the mechanical correlation of a huge number of items, and how desirable is the development and discussion of working hypotheses and the selection of a limited number of variables for study. Professor Macfie Campbell and his colleagues have been impressed during the research by the inadequacies in clinical records. These points are expanded in the various papers, which indicate that a strict investigation of this sort may at first appear to increase the difficulties of psychiatry by disposing of some easy generalizations and widely held assumptions, while clearing the way for further study and establishing some important correlations. There is in this collection very little that is new or surprising, but it is valuable for the critical outlook which informs the articles and the method of research pursued.

Life and Soul : Outlines of a Future Theoretical Physiology and of a Critical Philosophy. By MAX LOEWENTHAL. London : Allen and Unwin. 1934. Pp. 291. Price 8s. 6d.

The author of this work offers an interpretation of vital phenomena in which the conceptions are partly those of physics and partly of philosophy. His argument is clearly presented and well-knit but quite speculative, sometimes at variance with current physics and philosophy, and insufficiently related to the central problem here discussed though not clearly stated. His views on the spacial properties of psychic images seem untenable. The introductory chapter, in the first part of the book, deals with cellular structure and physiology, the next chapter with the general properties of living matter, and the third with chemical dynamics. There is a brief historical survey and then comes the second part in which philosophical considerations as to the outer and inner world are brought into the writer's general scheme.

Psychotherapie : Ein Lehrbuch für Studierende und Aerzte. Von H. KOGERER. Wien : Wilhelm Maudrich. 1934. Pp. 167. Price Rm. 10.

As in almost all manuals of psychotherapy there is here much more about psychopathology than about actual therapy. The reader seeks in a work with this title for advice as to the technique of treatment, the indications, the risks

and the methods, but he finds only fifty-five pages dealing with these subjects, while there are thirty-three on the causes of mental disorder and seventy on the symptoms, mechanisms, and other clinical features of such illness. In this last clinical section there are also brief incidental references to psychotherapy, but the work as a whole is really a cursory textbook of psychiatry written from the standpoint of a psychotherapist who deals mainly with neuroses. The sections on treatment are sensible and are based on much experience. The customary half-historical, half-critical survey of the various European schools of interpretative morbid psychology is well done, though nowadays tedious through repetition. The many illustrative case histories are interesting as showing the author's material, methods and success.

Les Encephalities Psychosiques. Par L. MARCHAND et A. COURTOIS. Paris: Le François. 1935. Pp. 144. Price 25 fr.

The authors deal here with forms of cerebral infection which manifest themselves predominantly or only by mental symptoms. Their course may he acute, subacute or chronic, and while most are probably infective, in others intoxications or disturbances of metabolism may be the causal factors. Inflammatory changes can be generally demonstrated in the brain or its membranes in patients who succumb in the acute phases of the disease. The so-called Acute Delirious Mania is perhaps the commonest and best defined of the acute conditions, but other cases follow childbirth, surgical operations, and local or general infections as acute rheumatism or influenza. The large proportion of cases which occur among the insane is very striking. Emphasis is laid on the high figure of the blood urea which is almost constant.

The symptoms and the pathological changes in both the acute and chronic forms are excellently described in this small volume, which is undoubtedly a valuable contribution to a subject which has scarcely received the attention it deserves.

The Problem of Mental Disorder. A Study undertaken by the Committee on Psychiatric Investigations, National Research Council. Edited by M. Bentley and E. V. Cowdry. London: McGraw Hill Publishing Co. 1934. Pp. 388. Price 24s.

This account of the present outlook for research in mental disorder has greater scope and authority than any other work on the subject in English. The difficulty of the problem is frankly recognized; no attempt is made to extenuate our present ignorance and impotence with regard to a great deal of mental illness. The editors are not psychiatrists, but they have enlisted some of the foremost workers in this field in the United States, so that in the first part of the book Professor Macfie Campbell, Professor Adolf Meyer, Dr. Wechsler, Dr. Myerson and Dr. Kubie present different aspects of the clinical

point of view. Dr. Kubie is a persuasive and modest representative of psychoanalysis. Apart from his contribution there is throughout the book evidence and even plain statement of a general impatience with the extreme claims of the psychoanalysts, unsupported as they are by any acceptable evidence. The second part of the book consists of papers on physiology, anatomy, biochemistry, biology and genetics, nutrition, endocrinology, psychology, pharmacology and anthropology, in which the bearing of such studies on the central theme is surveyed. Among the contributors here are Cobb, Cowdry, Penfield, Judson, Herrick, Minot, Yerkes, Bentley and other scientists of repute. In the face of the eager, not to say unprincipled, claims occasionally made for some individual method of study or treatment, it is salutary to have so honest, authoritative and hopeful a survey as that contained in this symposium.

Hallucinations et Délire. Les Formes Hallucinatoires de l'Automatisme Verbal. Par H. Ey. Paris: Félix Alcan. 1934. Pp. 192. Price 15 fr.

Dr. Ey brings together very clearly in this little book the views expressed in earlier papers which attracted attention among those interested in the problem of hallucinations. It is with psychomotor hallucinatory experiences that he is especially concerned. Discarding any atomistic view, he sees these as part of the whole delusional disorder, as an active expression of the patient's personality. It is upon the "error" rather than the sensory quality in the hallucination that he insists; he considers it the result of a fall in the psychic level determined by organic or by affective factors. After an introduction in which the notion of automatism in psychopathology is examined, there are chapters on the relation of hallucinations to images, language and inner speech, as well as on feelings of influence and passivity. The writer's views are put forward soberly and convincingly.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

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EDITOR.